

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : C12N 15/12, C07K 14/47, C12N 5/10, C07K 16/18, C12N 15/62, C12Q 1/68, G01N 33/50, 33/53, A61K 38/02, 48/00		A2	(11) International Publication Number: WO 00/37643 (43) International Publication Date: 29 June 2000 (29.06.00)
(21) International Application Number: PCT/US99/30909 (22) International Filing Date: 23 December 1999 (23.12.99) (30) Priority Data: 09/221,298 23 December 1998 (23.12.98) US 09/347,496 2 July 1999 (02.07.99) US 09/401,064 22 September 1999 (22.09.99) US 09/444,242 19 November 1999 (19.11.99) US 09/454,150 2 December 1999 (02.12.99) US (71) Applicant (for all designated States except US): CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): XU, Jiangchun [US/US]; 15805 SE 43rd Place, Bellevue, WA 98006 (US). LODES, Michael, J. [US/US]; 9223 - 36th Avenue SW, Seattle, WA 98126 (US). SECRIST, Heather [US/US]; 3844 - 35th Avenue West, Seattle, WA 98199 (US). BENSON, Darin, R. [US/US]; 723 N. 48th Street, Seattle, WA 98104 (US). MEAGHER, Madeleine, Joy [US/US]; 3819 Interlake Avenue N., Seattle, WA 98103 (US). STOLK, John [US/US]; 7436 NE 144th Place, Bothell, WA 98011		(US). WANG, Tongtong [CN/US]; 8049 NE 28th Street, Medina, WA 98039 (US). YUQIU, Jiang [CN/US]; 5001 South 232nd Street, Kent, WA 98032 (US). (74) Agents: MAKI, David, J. et al.; Seed and Berry LLP, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 (US). (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>	
(54) Title: COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE			
(57) Abstract Compositions and methods for the therapy and diagnosis of cancer, such as colon cancer, are disclosed. Compositions may comprise one or more colon tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a colon tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as colon cancer. Diagnostic methods based on detecting a colon tumor protein, or mRNA encoding such a protein, in a sample are also provided.			

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

WO 00/37643

PCT/US99/30909

COMPOUNDS FOR IMMUNOTHERAPY AND DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE

TECHNICAL FIELD

5 The present invention relates generally to therapy and diagnosis of cancer, such as colon cancer. The invention is more specifically related to polypeptides comprising at least a portion of a colon tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of colon cancer, and for the
10 diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

 Cancer is a significant health problem throughout the world. Although advances have been made in detection and therapy of cancer, no vaccine or other universally successful method for prevention or treatment is currently available. Current therapies, which
15 are generally based on a combination of chemotherapy or surgery and radiation, continue to prove inadequate in many patients.

 Colon cancer is the second most frequently diagnosed malignancy in the United States as well as the second most common cause of cancer death. An estimated 95,600 new cases of colon cancer will be diagnosed in 1998, with an estimated 47,700 deaths.
20 The five-year survival rate for patients with colorectal cancer detected in an early localized stage is 92%; unfortunately, only 37% of colorectal cancer is diagnosed at this stage. The survival rate drops to 64% if the cancer is allowed to spread to adjacent organs or lymph nodes, and to 7% in patients with distant metastases.

 The prognosis of colon cancer is directly related to the degree of penetration of
25 the tumor through the bowel wall and the presence or absence of nodal involvement, consequently, early detection and treatment are especially important. Currently, diagnosis is aided by the use of screening assays for fecal occult blood, sigmoidoscopy, colonoscopy and double contrast barium enemas. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. Recurrence
30 following surgery (the most common form of therapy) is a major problem and is often the

WO 00/37643

2

PCT/US99/30909

ultimate cause of death. In spite of considerable research into therapies for the disease, colon cancer remains difficult to diagnose and treat. In spite of considerable research into therapies for these and other cancers, colon cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as colon cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a colon tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises a sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in SEQ ID NO: 1-121, 123-197 and 205-486; (b) variants of a sequence recited in SEQ ID NO: 1-121, 123-197 and 205-486; and (c) complements of a sequence of (a) or (b).

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a colon tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a colon tumor protein; and (b) a physiologically acceptable carrier.

WO 00/37643

3

PCT/US99/30909

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5 Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10 Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an
15 immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for
20 removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of
25 a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a
30 polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under

WO 00/37643

4

PCT/US99/30909

conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective
5 amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a colon tumor protein; (ii) a polynucleotide encoding such a
10 polypeptide; and (iii) an antigen-presenting cell that expresses such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining
15 the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred
20 embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be colon cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding
25 agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

30 The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a)

contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached figures. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

SEQUENCE IDENTIFIERS

SEQ ID NO: 1 is a first determined cDNA sequence for Contig 1, showing homology to Neutrophil Gelatinase Associated Lipocalin.

SEQ ID NO: 2 is the determined cDNA sequence for Contig 2, showing no significant homology to any known genes.

SEQ ID NO: 3 is the determined cDNA sequence for Contig 4, showing homology to Carcinoembryonic antigen.

5 SEQ ID NO: 4 is the determined cDNA sequence for Contig 5, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 5 is the determined cDNA sequence for Contig 9, showing homology to Carcinoembryonic antigen.

10 SEQ ID NO: 6 is the determined cDNA sequence for Contig 52, showing homology to Carcinoembryonic antigen.

SEQ ID NO: 7 is the determined cDNA sequence for Contig 6, showing homology to Villin.

SEQ ID NO: 8 is the determined cDNA sequence for Contig 8, showing no significant homology to any known genes.

15 SEQ ID NO: 9 is the determined cDNA sequence for Contig 10, showing homology to Transforming Growth Factor (BIGH3).

SEQ ID NO: 10 is the determined cDNA sequence for Contig 19, showing homology to Transforming Growth Factor (BIGH3).

20 SEQ ID NO: 11 is the determined cDNA sequence for Contig 21, showing homology to Transforming Growth Factor (BIGH3).

SEQ ID NO: 12 is the determined cDNA sequence for Contig 11, showing homology to CO-029.

SEQ ID NO: 13 is the determined cDNA sequence for Contig 55, showing homology to CO-029.

25 SEQ ID NO: 14 is the determined cDNA sequence for Contig 12, showing homology to Chromosome 17, clone hRPC.1171_I_10, also referred to as C798P.

SEQ ID NO: 15 is the determined cDNA sequence for Contig 13, showing no significant homology to any known gene.

30 SEQ ID NO: 16 is the determined cDNA sequence for Contig 14, also referred to as 14261, showing no significant homology to any known gene.

30 SEQ ID NO: 31 is the determined cDNA sequence for Contig 30, showing homology to Zinc Finger Transcription Factor (ZNF207).

WO 00/37643

8

PCT/US99/30909

SEQ ID NO: 32 is the determined cDNA sequence for Contig 31, showing no significant homology to any known gene, but partial homology to *Mus musculus* GOB-4 homolog.

SEQ ID NO: 33 is the determined cDNA sequence for Contig 35, showing no significant homology to any known gene, but partial homology to *Mus musculus* GOB-4 homolog.

SEQ ID NO: 34 is the determined cDNA sequence for Contig 32, showing no significant homology to any known gene.

SEQ ID NO: 35 is the determined cDNA sequence for Contig 34, showing homology to Desmoglein 2.

SEQ ID NO: 36 is the determined cDNA sequence for Contig 36, showing no significant homology to any known gene.

SEQ ID NO: 37 is the determined cDNA sequence for Contig 37, showing homology to Putative Transmembrane Protein.

SEQ ID NO: 38 is the determined cDNA sequence for Contig 38, also referred to as C796P and 14219, showing no significant homology to any known gene.

SEQ ID NO: 39 is the determined cDNA sequence for Contig 40, showing homology to Nonspecific Cross-reacting Antigen.

SEQ ID NO: 40 is the determined cDNA sequence for Contig 41, also referred to as C799P and 14308, showing no significant homology to any known gene.

SEQ ID NO: 41 is the determined cDNA sequence for Contig 42, also referred to as C794P and 14309, showing no significant homology to any known gene.

SEQ ID NO: 42 is the determined cDNA sequence for Contig 43, showing homology to Chromosome 1 specific transcript KIAA0487.

SEQ ID NO: 43 is the determined cDNA sequence for Contig 45, showing homology to hMCM2.

SEQ ID NO: 44 is the determined cDNA sequence for Contig 46, showing homology to ETS2.

SEQ ID NO: 45 is the determined cDNA sequence for Contig 49, showing homology to Pump-1.

SEQ ID NO: 46 is the determined cDNA sequence for Contig 50, also referred to as C792P and 18323, showing no significant homology to any known gene.

SEQ ID NO: 47 is the determined cDNA sequence for Contig 51, also referred to as C795P and 14317, showing no significant homology to any known gene.

5 SEQ ID NO: 48 is the determined cDNA sequence for 11092, showing no significant
homology to any known gene.

SEQ ID NO: 49 is the determined cDNA sequence for 11093, showing no significant homology to any known gene.

10 SEQ ID NO: 50 is the determined cDNA sequence for 11094, showing homology
Human Putative Enterocyte Differentiation Protein.

SEQ ID NO: 51 is the determined cDNA sequence for 11095, showing homology to Human Transcriptional Corepressor hKAP1/TIF1B mRNA.

SEQ ID NO: 52 is the determined cDNA sequence for 11096, showing no significant homology to any known gene.

15 SEQ ID NO: 53 is the determined cDNA sequence for 11097, showing homology to Human Nonspecific Antigen.

SEQ ID NO: 54 is the determined cDNA sequence for 11098, showing no significant homology to any known gene.

SEQ ID NO: 55 is the determined cDNA sequence for 11099, showing homology to
20 Human Pancreatic Secretory Inhibitor (PST) mRNA.

SEQ ID NO: 56 is the determined cDNA sequence for 11186, showing homology to Human Pancreatic Secretory Inhibitor (PST) mRNA.

SEQ ID NO: 57 is the determined cDNA sequence for 11101, showing homology to Human Chromosome X.

25 SEQ ID NO. 58 is the determined cDNA sequence for 11102, showing homology to Human Chromosome X.

SEQ ID NO: 59 is the determined cDNA sequence for 11103, showing no significant homology to any known gene.

SEQ ID NO: 60 is the determined cDNA sequence for 11174, showing no significant
30 homology to any known gene.

SEQ ID NO: 61 is the determined cDNA sequence for 11104, showing homology to Human mRNA for KIAA0154.

SEQ ID NO: 62 is the determined cDNA sequence for 11105, showing homology to Human Apurinic/Apyrimidinic Endonuclease (hap1)mRNA.

5 SEQ ID NO: 63 is the determined cDNA sequence for 11106, showing homology to Human Chromosome 12p13.

SEQ ID NO: 64 is the determined cDNA sequence for 11107, showing homology to Human 90 kDa Heat Shock Protein.

10 SEQ ID NO: 65 is the determined cDNA sequence for 11108, showing no significant homology to any known gene.

SEQ ID NO: 66 is the determined cDNA sequence for 11112, showing no significant homology to any known gene.

SEQ ID NO: 67 is the determined cDNA sequence for 11115, showing no significant homology to any known gene.

15 SEQ ID NO: 68 is the determined cDNA sequence for 11117, showing no significant homology to any known gene.

SEQ ID NO: 69 is the determined cDNA sequence for 11118, showing no significant homology to any known gene.

20 SEQ ID NO: 70 is the determined cDNA sequence for 11119, showing homology to Human Elongation Factor 1-alpha.

SEQ ID NO: 71 is the determined cDNA sequence for 11121, showing homology to Human Lamin B Receptor (LBR) mRNA.

SEQ ID NO: 72 is the determined cDNA sequence for 11122, showing homology to H. sapiens mRNA for Novel Glucocorticoid.

25 SEQ ID NO: 73 is the determined cDNA sequence for 11123, showing homology to H. sapiens mRNA for snRNP protein B.

SEQ ID NO: 74 is the determined cDNA sequence for 11124, showing homology to Human Cisplatin Resistance Associated Beta-protein.

30 SEQ ID NO: 75 is the determined cDNA sequence for 11127, showing homology to M. musculus Calumenin mRNA.

WO 00/37643

11

PCT/US99/30909

SEQ ID NO: 76 is the determined cDNA sequence for 11128, showing homology to Human ras-related small GTP binding protein.

SEQ ID NO: 77 is the determined cDNA sequence for 11130, showing homology to Human Cosmid U169d2.

5 SEQ ID NO: 78 is the determined cDNA sequence for 11131, showing homology to H. sapiens mRNA for protein homologous to Elongation 1-g.

SEQ ID NO: 79 is the determined cDNA sequence for 11134, showing no significant homology to any known gene.

10 SEQ ID NO: 80 is the determined cDNA sequence for 11135, showing homology to H. sapiens Nieman-Pick (NPC1) mRNA.

SEQ ID NO: 81 is the determined cDNA sequence for 11137, showing homology to H. sapiens mRNA for Niecin b-chain.

SEQ ID NO: 82 is the determined cDNA sequence for 11138, showing homology to Human Endogenous Retroviral Protease mRNA.

15 SEQ ID NO: 83 is the determined cDNA sequence for 11139, showing homology to H. sapiens mRNA for DMBT1 protein.

SEQ ID NO: 84 is the determined cDNA sequence for 11140, showing homology to H. sapiens ras GTPase activating-like protein.

20 SEQ ID NO: 85 is the determined cDNA sequence for 11143, showing homology to Human Acidic Ribosomal Phosphoprotein PO mRNA.

SEQ ID NO: 86 is the determined cDNA sequence for 11144, showing homology to H. sapiens U21 mRNA.

SEQ ID NO: 87 is the determined cDNA sequence for 11145, showing homology to Human GTP-binding protein.

25 SEQ ID NO: 88 is the determined cDNA sequence for 11148, showing homology to H. sapiens U21 mRNA.

SEQ ID NO: 89 is the determined cDNA sequence for 11151, showing no significant homology to any known gene.

30 SEQ ID NO: 90 is the determined cDNA sequence for 11154, showing no significant homology to any known gene.

WO 00/37643

12

PCT/US99/30909

SEQ ID NO: 91 is the determined cDNA sequence for 11156, showing homology to H. sapiens Ribosomal Protein L27.

SEQ ID NO: 92 is the determined cDNA sequence for 11157, showing homology to H. sapiens Ribosomal Protein L27.

5 SEQ ID NO: 93 is the determined cDNA sequence for 11158, showing no significant homology to any known gene.

SEQ ID NO: 94 is the determined cDNA sequence for 11162, showing homology to Ag-X antigen.

10 SEQ ID NO: 95 is the determined cDNA sequence for 11164, showing homology to H. sapiens mRNA for Signal Recognition Protein sub14.

SEQ ID NO: 96 is the determined cDNA sequence for 11165, showing homology to Human PAC 204e5/127h14.

SEQ ID NO: 97 is the determined cDNA sequence for 11166, showing homology to Human mRNA for KIAA0108.

15 SEQ ID NO: 98 is the determined cDNA sequence for 11167, showing homology to H. sapiens mRNA for Neutrophil Gelatinase asst. Lipocalin.

SEQ ID NO: 99 is the determined cDNA sequence for 11168, showing no significant homology to any known gene.

20 SEQ ID NO: 100 is the determined cDNA sequence for 11172, showing no significant homology to any known gene.

SEQ ID NO: 101 is the determined cDNA sequence for 11175, showing no significant homology to any known gene.

SEQ ID NO: 102 is the determined cDNA sequence for 11176, showing homology to Human maspin mRNA.

25 SEQ ID NO: 103 is the determined cDNA sequence for 11177, showing homology to Human Carcinoembryonic Antigen.

SEQ ID NO: 104 is the determined cDNA sequence for 11178, showing homology to Human A-Tubulin mRNA.

30 SEQ ID NO: 105 is the determined cDNA sequence for 11179, showing homology to Human mRNA for proton-ATPase-like protein.

WO 00/37643

13

PCT/US99/30909

SEQ ID NO: 106 is the determined cDNA sequence for 11180, showing homology to Human HepG2 3' region cDNA clone hmd.

SEQ ID NO: 107 is the determined cDNA sequence for 11182, showing homology to Human MHC homologous to Chicken B-Complex Protein.

5 SEQ ID NO: 108 is the determined cDNA sequence for 11183, showing homology to Human High Mobility Group Box (SSRP1) mRNA.

SEQ ID NO: 109 is the determined cDNA sequence for 11184, showing no significant homology to any known gene.

10 SEQ ID NO: 110 is the determined cDNA sequence for 11185, showing no significant homology to any known gene.

SEQ ID NO: 111 is the determined cDNA sequence for 11187, showing no significant homology to any known gene.

SEQ ID NO: 112 is the determined cDNA sequence for 11190, showing homology to Human Replication Protein A 70kDa.

15 SEQ ID NO: 113 is the determined cDNA sequence for Contig 47, also referred to as C797P, showing homology to Human Chromosome X clone bWXd342.

SEQ ID NO: 114 is the determined cDNA sequence for Contig 7, showing homology to Equilibrative Nucleoside Transporter 2 (ent2).

20 SEQ ID NO: 115 is the determined cDNA sequence for 14235.1, also referred to as C791P, showing homology to H. sapiens chromosome 21 derived BAC containing ets-2 gene.

SEQ ID NO: 116 is the determined cDNA sequence for 14287.2, showing no significant homology to any known gene, but some degree of homology to Putative Transmembrane Protein.

25 SEQ ID NO: 117 is the determined cDNA sequence for 14233.1, also referred to as Contig 48, showing no significant homology to any known gene.

SEQ ID NO: 118 is the determined cDNA sequence for 14298.2, also referred to as C793P, showing no significant homology to any known gene.

30 SEQ ID NO: 119 is the determined cDNA sequence for 14372, also referred to as Contig 44, showing no significant homology to any known gene.

WO 00/37643

14

PCT/US99/30909

SEQ ID NO: 120 is the determined cDNA sequence for 14295, showing homology to secreted cement gland protein XAG-2 homolog.

SEQ ID NO: 121 is the determined full-length cDNA sequence for a clone showing homology to Beta IG-H3.

5 SEQ ID NO: 122 is the predicted amino acid sequence for the clone of SEQ ID NO: 121.

SEQ ID NO: 123 is a longer determined cDNA sequence for C751P.

SEQ ID NO: 124 is a longer determined cDNA sequence for C791P.

SEQ ID NO: 125 is a longer determined cDNA sequence for C792P.

10 SEQ ID NO: 126 is a longer determined cDNA sequence for C793P.

SEQ ID NO: 127 is a longer determined cDNA sequence for C794P.

SEQ ID NO: 128 is a longer determined cDNA sequence for C795P.

SEQ ID NO: 129 is a longer determined cDNA sequence for C796P.

SEQ ID NO: 130 is a longer determined cDNA sequence for C797P.

15 SEQ ID NO: 131 is a longer determined cDNA sequence for C798P.

SEQ ID NO: 132 is a longer determined cDNA sequence for C799P.

SEQ ID NO: 133 is a first partial determined cDNA sequence for CoSub-3 (also known as 23569).

20 SEQ ID NO: 134 is a second partial determined cDNA sequence for CoSub-3 (also known as 23569).

SEQ ID NO: 135 is a first partial determined cDNA sequence for CoSub-13 (also known as 23579).

SEQ ID NO: 136 is a second partial determined cDNA sequence for CoSub-13 (also known as 23579).

25 SEQ ID NO: 137 is the determined cDNA sequence for CoSub-17 (also known as 23583).

SEQ ID NO: 138 is the determined cDNA sequence for CoSub-19 (also known as 23585).

30 SEQ ID NO: 139 is the determined cDNA sequence for CoSub-22 (also known as 23714).

SEQ ID NO: 158 is the determined cDNA sequence for CT13 (also known as 24111).

WO 00/37643

16

PCT/US99/30909

SEQ ID NO: 159 is the determined cDNA sequence for CT14 (also known as 24112).
 SEQ ID NO: 160 is the determined cDNA sequence for CT15 (also known as 24113).
 SEQ ID NO: 161 is the determined cDNA sequence for CT17 (also known as 24115).
 SEQ ID NO: 162 is the determined cDNA sequence for CT18 (also known as 24116).
 5 SEQ ID NO: 163 is the determined cDNA sequence for CT22 (also known as 23848).
 SEQ ID NO: 164 is the determined cDNA sequence for CT24 (also known as 23849).
 SEQ ID NO: 165 is the determined cDNA sequence for CT31 (also known as 23854).
 SEQ ID NO: 166 is the determined cDNA sequence for CT34 (also known as 23856).
 SEQ ID NO: 167 is the determined cDNA sequence for CT37 (also known as 23859).
 10 SEQ ID NO: 168 is the determined cDNA sequence for CT39 (also known as 23860).
 SEQ ID NO: 169 is the determined cDNA sequence for CT40 (also known as 23861).
 SEQ ID NO: 170 is the determined cDNA sequence for CT51 (also known as 24130).
 SEQ ID NO: 171 is the determined cDNA sequence for CT53 (also known as 24132).
 SEQ ID NO: 172 is the determined cDNA sequence for CT63 (also known as 24595).
 15 SEQ ID NO: 173 is the determined cDNA sequence for CT88 (also known as 24608).
 SEQ ID NO: 174 is the determined cDNA sequence for CT92 (also known as 24800).
 SEQ ID NO: 175 is the determined cDNA sequence for CT94 (also known as 24802).
 SEQ ID NO: 176 is the determined cDNA sequence for CT102 (also known as
 24805).
 20 SEQ ID NO: 177 is the determined cDNA sequence for CT103 (also known as
 24806).
 SEQ ID NO: 178 is the determined cDNA sequence for CT111 (also known as
 25520).
 SEQ ID NO: 179 is the determined cDNA sequence for CT118 (also known as
 25 25522).
 SEQ ID NO: 180 is the determined cDNA sequence for CT121 (also known as
 25523).
 SEQ ID NO: 181 is the determined cDNA sequence for CT126 (also known as
 25527).
 30 SEQ ID NO: 182 is the determined cDNA sequence for CT135 (also known as
 25534).

WO 00/37643

17

PCT/US99/30909

SEQ ID NO: 183 is the determined cDNA sequence for CT140 (also known as 25537).

SEQ ID NO: 184 is the determined cDNA sequence for CT145 (also known as 25542).

5 SEQ ID NO: 185 is the determined cDNA sequence for CT147 (also known as 25543).

SEQ ID NO: 186 is the determined cDNA sequence for CT148 (also known as 25544).

10 SEQ ID NO: 187 is the determined cDNA sequence for CT502 (also known as 26420).

SEQ ID NO: 188 is the determined cDNA sequence for CT507 (also known as 26425).

SEQ ID NO: 189 is the determined cDNA sequence for CT521 (also known as 27366).

15 SEQ ID NO: 190 is the determined cDNA sequence for CT544 (also known as 27375).

SEQ ID NO: 191 is the determined cDNA sequence for CT577 (also known as 27385).

20 SEQ ID NO: 192 is the determined cDNA sequence for CT580 (also known as 27387).

SEQ ID NO: 193 is the determined cDNA sequence for CT594 (also known as 27540).

SEQ ID NO: 194 is the determined cDNA sequence for CT606 (also known as 27547).

25 SEQ ID NO: 195 is the determined cDNA sequence for CT607 (also known as 27548).

SEQ ID NO: 196 is the determined cDNA sequence for CT599 (also known as 27903).

30 SEQ ID NO: 197 is the determined cDNA sequence for CT632 (also known as 27922).

SEQ ID NO: 198 is the predicted amino acid sequence for CT502 (SEQ ID NO: 187).

WO 00/37643

18

PCT/US99/30909

SEQ ID NO: 199 is the predicted amino acid sequence for CT507 (SEQ ID NO: 188).
SEQ ID NO: 200 is the predicted amino acid sequence for CT521 (SEQ ID NO: 189).
SEQ ID NO: 201 is the predicted amino acid sequence for CT544 (SEQ ID NO: 190).
SEQ ID NO: 202 is the predicted amino acid sequence for CT606 (SEQ ID NO: 194).
5 SEQ ID NO: 203 is the predicted amino acid sequence for CT607 (SEQ ID NO: 195).
SEQ ID NO: 204 is the predicted amino acid sequence for CT632 (SEQ ID NO: 197).
SEQ ID NO: 205 is the determined cDNA sequence for clone 25244.
SEQ ID NO: 206 is the determined cDNA sequence for clone 25245.
SEQ ID NO: 207 is the determined cDNA sequence for clone 25246.
10 SEQ ID NO: 208 is the determined cDNA sequence for clone 25248.
SEQ ID NO: 209 is the determined cDNA sequence for clone 25249.
SEQ ID NO: 210 is the determined cDNA sequence for clone 25250.
SEQ ID NO: 211 is the determined cDNA sequence for clone 25251.
SEQ ID NO: 212 is the determined cDNA sequence for clone 25252.
15 SEQ ID NO: 213 is the determined cDNA sequence for clone 25253.
SEQ ID NO: 214 is the determined cDNA sequence for clone 25254.
SEQ ID NO: 215 is the determined cDNA sequence for clone 25255.
SEQ ID NO: 216 is the determined cDNA sequence for clone 25256.
SEQ ID NO: 217 is the determined cDNA sequence for clone 25257.
20 SEQ ID NO: 218 is the determined cDNA sequence for clone 25259.
SEQ ID NO: 219 is the determined cDNA sequence for clone 25260.
SEQ ID NO: 220 is the determined cDNA sequence for clone 25261.
SEQ ID NO: 221 is the determined cDNA sequence for clone 25262.
SEQ ID NO: 222 is the determined cDNA sequence for clone 25263.
25 SEQ ID NO: 223 is the determined cDNA sequence for clone 25264.
SEQ ID NO: 224 is the determined cDNA sequence for clone 25265.
SEQ ID NO: 225 is the determined cDNA sequence for clone 25266.
SEQ ID NO: 226 is the determined cDNA sequence for clone 25267.
SEQ ID NO: 227 is the determined cDNA sequence for clone 25268.
30 SEQ ID NO: 228 is the determined cDNA sequence for clone 25269.
SEQ ID NO: 229 is the determined cDNA sequence for clone 25271.

WO 00/37643

19

PCT/US99/30909

SEQ ID NO: 230 is the determined cDNA sequence for clone 25272.
SEQ ID NO: 231 is the determined cDNA sequence for clone 25273.
SEQ ID NO: 232 is the determined cDNA sequence for clone 25274.
SEQ ID NO: 233 is the determined cDNA sequence for clone 25275.
5 SEQ ID NO: 234 is the determined cDNA sequence for clone 25276.
SEQ ID NO: 235 is the determined cDNA sequence for clone 25277.
SEQ ID NO: 236 is the determined cDNA sequence for clone 25278.
SEQ ID NO: 237 is the determined cDNA sequence for clone 25280.
SEQ ID NO: 238 is the determined cDNA sequence for clone 25281.
10 SEQ ID NO: 239 is the determined cDNA sequence for clone 25282.
SEQ ID NO: 240 is the determined cDNA sequence for clone 25283.
SEQ ID NO: 241 is the determined cDNA sequence for clone 25284.
SEQ ID NO: 242 is the determined cDNA sequence for clone 25285.
SEQ ID NO: 243 is the determined cDNA sequence for clone 25286.
15 SEQ ID NO: 244 is the determined cDNA sequence for clone 25287.
SEQ ID NO: 245 is the determined cDNA sequence for clone 25288.
SEQ ID NO: 246 is the determined cDNA sequence for clone 25289.
SEQ ID NO: 247 is the determined cDNA sequence for clone 25290.
SEQ ID NO: 248 is the determined cDNA sequence for clone 25291.
20 SEQ ID NO: 249 is the determined cDNA sequence for clone 25292.
SEQ ID NO: 250 is the determined cDNA sequence for clone 25293.
SEQ ID NO: 251 is the determined cDNA sequence for clone 25294.
SEQ ID NO: 252 is the determined cDNA sequence for clone 25295.
SEQ ID NO: 253 is the determined cDNA sequence for clone 25296.
25 SEQ ID NO: 254 is the determined cDNA sequence for clone 25297.
SEQ ID NO: 255 is the determined cDNA sequence for clone 25418.
SEQ ID NO: 256 is the determined cDNA sequence for clone 25419.
SEQ ID NO: 257 is the determined cDNA sequence for clone 25420.
SEQ ID NO: 258 is the determined cDNA sequence for clone 25421.
30 SEQ ID NO: 259 is the determined cDNA sequence for clone 25422.
SEQ ID NO: 260 is the determined cDNA sequence for clone 25423.

SEQ ID NO: 261 is the determined cDNA sequence for clone 25424.
SEQ ID NO: 262 is the determined cDNA sequence for clone 25426.
SEQ ID NO: 263 is the determined cDNA sequence for clone 25427.
SEQ ID NO: 264 is the determined cDNA sequence for clone 25428.
5 SEQ ID NO: 265 is the determined cDNA sequence for clone 25429.
SEQ ID NO: 266 is the determined cDNA sequence for clone 25430.
SEQ ID NO: 267 is the determined cDNA sequence for clone 25431.
SEQ ID NO: 268 is the determined cDNA sequence for clone 25432.
SEQ ID NO: 269 is the determined cDNA sequence for clone 25433.
10 SEQ ID NO: 270 is the determined cDNA sequence for clone 25434.
SEQ ID NO: 271 is the determined cDNA sequence for clone 25435.
SEQ ID NO: 272 is the determined cDNA sequence for clone 25436.
SEQ ID NO: 273 is the determined cDNA sequence for clone 25437.
SEQ ID NO: 274 is the determined cDNA sequence for clone 25438.
15 SEQ ID NO: 275 is the determined cDNA sequence for clone 25439.
SEQ ID NO: 276 is the determined cDNA sequence for clone 25440.
SEQ ID NO: 277 is the determined cDNA sequence for clone 25441.
SEQ ID NO: 278 is the determined cDNA sequence for clone 25442.
SEQ ID NO: 279 is the determined cDNA sequence for clone 25443.
20 SEQ ID NO: 280 is the determined cDNA sequence for clone 25444.
SEQ ID NO: 281 is the determined cDNA sequence for clone 25445.
SEQ ID NO: 282 is the determined cDNA sequence for clone 25446.
SEQ ID NO: 283 is the determined cDNA sequence for clone 25447.
SEQ ID NO: 284 is the determined cDNA sequence for clone 25448.
25 SEQ ID NO: 285 is the determined cDNA sequence for clone 25844.
SEQ ID NO: 286 is the determined cDNA sequence for clone 25845.
SEQ ID NO: 287 is the determined cDNA sequence for clone 25846.
SEQ ID NO: 288 is the determined cDNA sequence for clone 25847.
SEQ ID NO: 289 is the determined cDNA sequence for clone 25848.
30 SEQ ID NO: 290 is the determined cDNA sequence for clone 25850.
SEQ ID NO: 291 is the determined cDNA sequence for clone 25851.

WO 00/37643

21

PCT/US99/30909

SEQ ID NO: 292 is the determined cDNA sequence for clone 25852.
SEQ ID NO: 293 is the determined cDNA sequence for clone 25853.
SEQ ID NO: 294 is the determined cDNA sequence for clone 25854.
SEQ ID NO: 295 is the determined cDNA sequence for clone 25855.
5 SEQ ID NO: 296 is the determined cDNA sequence for clone 25856.
SEQ ID NO: 297 is the determined cDNA sequence for clone 25857.
SEQ ID NO: 298 is the determined cDNA sequence for clone 25858.
SEQ ID NO: 299 is the determined cDNA sequence for clone 25859.
SEQ ID NO: 300 is the determined cDNA sequence for clone 25860.
10 SEQ ID NO: 301 is the determined cDNA sequence for clone 25861.
SEQ ID NO: 302 is the determined cDNA sequence for clone 25862.
SEQ ID NO: 303 is the determined cDNA sequence for clone 25863.
SEQ ID NO: 304 is the determined cDNA sequence for clone 25864.
SEQ ID NO: 305 is the determined cDNA sequence for clone 25865.
15 SEQ ID NO: 306 is the determined cDNA sequence for clone 25866.
SEQ ID NO: 307 is the determined cDNA sequence for clone 25867.
SEQ ID NO: 308 is the determined cDNA sequence for clone 25868.
SEQ ID NO: 309 is the determined cDNA sequence for clone 25869.
SEQ ID NO: 310 is the determined cDNA sequence for clone 25870.
20 SEQ ID NO: 311 is the determined cDNA sequence for clone 25871.
SEQ ID NO: 312 is the determined cDNA sequence for clone 25872.
SEQ ID NO: 313 is the determined cDNA sequence for clone 25873.
SEQ ID NO: 314 is the determined cDNA sequence for clone 25875.
SEQ ID NO: 315 is the determined cDNA sequence for clone 25876.
25 SEQ ID NO: 316 is the determined cDNA sequence for clone 25877.
SEQ ID NO: 317 is the determined cDNA sequence for clone 25878.
SEQ ID NO: 318 is the determined cDNA sequence for clone 25879.
SEQ ID NO: 319 is the determined cDNA sequence for clone 25880.
SEQ ID NO: 320 is the determined cDNA sequence for clone 25881.
30 SEQ ID NO: 321 is the determined cDNA sequence for clone 25882.
SEQ ID NO: 322 is the determined cDNA sequence for clone 25883.

SEQ ID NO: 323 is the determined cDNA sequence for clone 25884.
SEQ ID NO: 324 is the determined cDNA sequence for clone 25885.
SEQ ID NO: 325 is the determined cDNA sequence for clone 25886.
SEQ ID NO: 326 is the determined cDNA sequence for clone 25887.
5 SEQ ID NO: 327 is the determined cDNA sequence for clone 25888.
SEQ ID NO: 328 is the determined cDNA sequence for clone 25889.
SEQ ID NO: 329 is the determined cDNA sequence for clone 25890.
SEQ ID NO: 330 is the determined cDNA sequence for clone 25892.
SEQ ID NO: 331 is the determined cDNA sequence for clone 25894.
10 SEQ ID NO: 332 is the determined cDNA sequence for clone 25895.
SEQ ID NO: 333 is the determined cDNA sequence for clone 25896.
SEQ ID NO: 334 is the determined cDNA sequence for clone 25897.
SEQ ID NO: 335 is the determined cDNA sequence for clone 25899.
SEQ ID NO: 336 is the determined cDNA sequence for clone 25900.
15 SEQ ID NO: 337 is the determined cDNA sequence for clone 25901.
SEQ ID NO: 338 is the determined cDNA sequence for clone 25902.
SEQ ID NO: 339 is the determined cDNA sequence for clone 25903.
SEQ ID NO: 340 is the determined cDNA sequence for clone 25904.
SEQ ID NO: 341 is the determined cDNA sequence for clone 25906.
20 SEQ ID NO: 342 is the determined cDNA sequence for clone 25907.
SEQ ID NO: 343 is the determined cDNA sequence for clone 25908.
SEQ ID NO: 344 is the determined cDNA sequence for clone 25909.
SEQ ID NO: 345 is the determined cDNA sequence for clone 25910.
SEQ ID NO: 346 is the determined cDNA sequence for clone 25911.
25 SEQ ID NO: 347 is the determined cDNA sequence for clone 25912.
SEQ ID NO: 348 is the determined cDNA sequence for clone 25913.
SEQ ID NO: 349 is the determined cDNA sequence for clone 25914.
SEQ ID NO: 350 is the determined cDNA sequence for clone 25915.
SEQ ID NO: 351 is the determined cDNA sequence for clone 25916.
30 SEQ ID NO: 352 is the determined cDNA sequence for clone 25917.
SEQ ID NO: 353 is the determined cDNA sequence for clone 25918.

WO 00/37643

23

PCT/US99/30909

SEQ ID NO: 354 is the determined cDNA sequence for clone 25919.
SEQ ID NO: 355 is the determined cDNA sequence for clone 25920.
SEQ ID NO: 356 is the determined cDNA sequence for clone 25921.
SEQ ID NO: 357 is the determined cDNA sequence for clone 25922.
5 SEQ ID NO: 358 is the determined cDNA sequence for clone 25924.
SEQ ID NO: 359 is the determined cDNA sequence for clone 25925.
SEQ ID NO: 360 is the determined cDNA sequence for clone 25926.
SEQ ID NO: 361 is the determined cDNA sequence for clone 25927.
SEQ ID NO: 362 is the determined cDNA sequence for clone 25928.
10 SEQ ID NO: 363 is the determined cDNA sequence for clone 25929.
SEQ ID NO: 364 is the determined cDNA sequence for clone 25930.
SEQ ID NO: 365 is the determined cDNA sequence for clone 25931.
SEQ ID NO: 366 is the determined cDNA sequence for clone 25932.
SEQ ID NO: 367 is the determined cDNA sequence for clone 25933.
15 SEQ ID NO: 368 is the determined cDNA sequence for clone 25934.
SEQ ID NO: 369 is the determined cDNA sequence for clone 25935.
SEQ ID NO: 370 is the determined cDNA sequence for clone 25936.
SEQ ID NO: 371 is the determined cDNA sequence for clone 25939.
SEQ ID NO: 372 is the determined cDNA sequence for clone 32016.
20 SEQ ID NO: 373 is the determined cDNA sequence for clone 32021.
SEQ ID NO: 374 is the determined cDNA sequence for clone 31993.
SEQ ID NO: 375 is the determined cDNA sequence for clone 31997.
SEQ ID NO: 376 is the determined cDNA sequence for clone 31942.
SEQ ID NO: 377 is the determined cDNA sequence for clone 31937.
25 SEQ ID NO: 378 is the determined cDNA sequence for clone 31952.
SEQ ID NO: 379 is the determined cDNA sequence for clone 31992.
SEQ ID NO: 380 is the determined cDNA sequence for clone 31961.
SEQ ID NO: 381 is the determined cDNA sequence for clone 31964.
SEQ ID NO: 382 is the determined cDNA sequence for clone 32005.
30 SEQ ID NO: 383 is the determined cDNA sequence for clone 31980.
SEQ ID NO: 384 is the determined cDNA sequence for clone 31940.

SEQ ID NO: 385 is the determined cDNA sequence for clone 32004.
SEQ ID NO: 386 is the determined cDNA sequence for clone 31956.
SEQ ID NO: 387 is the determined cDNA sequence for clone 31934.
SEQ ID NO: 388 is the determined cDNA sequence for clone 31998.
5 SEQ ID NO: 389 is the determined cDNA sequence for clone 31973.
SEQ ID NO: 390 is the determined cDNA sequence for clone 31976.
SEQ ID NO: 391 is the determined cDNA sequence for clone 31988.
SEQ ID NO: 392 is the determined cDNA sequence for clone 31948.
SEQ ID NO: 393 is the determined cDNA sequence for clone 32013.
10 SEQ ID NO: 394 is the determined cDNA sequence for clone 31986.
SEQ ID NO: 395 is the determined cDNA sequence for clone 31954.
SEQ ID NO: 396 is the determined cDNA sequence for clone 31987.
SEQ ID NO: 397 is the determined cDNA sequence for clone 32029.
SEQ ID NO: 398 is the determined cDNA sequence for clone 32028.
15 SEQ ID NO: 399 is the determined cDNA sequence for clone 32012.
SEQ ID NO: 400 is the determined cDNA sequence for clone 31959.
SEQ ID NO: 401 is the determined cDNA sequence for clone 32027.
SEQ ID NO: 402 is the determined cDNA sequence for clone 31957.
SEQ ID NO: 403 is the determined cDNA sequence for clone 31950.
20 SEQ ID NO: 404 is the determined cDNA sequence for clone 32011.
SEQ ID NO: 405 is the determined cDNA sequence for clone 32022.
SEQ ID NO: 406 is the determined cDNA sequence for clone 32014.
SEQ ID NO: 407 is the determined cDNA sequence for clone 31963.
SEQ ID NO: 408 is the determined cDNA sequence for clone 31989.
25 SEQ ID NO: 409 is the determined cDNA sequence for clone 32015.
SEQ ID NO: 410 is the determined cDNA sequence for clone 32002.
SEQ ID NO: 411 is the determined cDNA sequence for clone 31939.
SEQ ID NO: 412 is the determined cDNA sequence for clone 32003.
SEQ ID NO: 413 is the determined cDNA sequence for clone 31936.
30 SEQ ID NO: 414 is the determined cDNA sequence for clone 32007.
SEQ ID NO: 415 is the determined cDNA sequence for clone 31965.

SEQ ID NO: 416 is the determined cDNA sequence for clone 31935.
SEQ ID NO: 417 is the determined cDNA sequence for clone 32008.
SEQ ID NO: 418 is the determined cDNA sequence for clone 31966.
SEQ ID NO: 419 is the determined cDNA sequence for clone 32020.
5 SEQ ID NO: 420 is the determined cDNA sequence for clone 31971.
SEQ ID NO: 421 is the determined cDNA sequence for clone 31977.
SEQ ID NO: 422 is the determined cDNA sequence for clone 31985.
SEQ ID NO: 423 is the determined cDNA sequence for clone 32023.
SEQ ID NO: 424 is the determined cDNA sequence for clone 31981.
10 SEQ ID NO: 425 is the determined cDNA sequence for clone 32006.
SEQ ID NO: 426 is the determined cDNA sequence for clone 31991.
SEQ ID NO: 427 is the determined cDNA sequence for clone 31995.
SEQ ID NO: 428 is the determined cDNA sequence for clone 32000.
SEQ ID NO: 429 is the determined cDNA sequence for clone 31990.
15 SEQ ID NO: 430 is the determined cDNA sequence for clone 31946.
SEQ ID NO: 431 is the determined cDNA sequence for clone 31938.
SEQ ID NO: 432 is the determined cDNA sequence for clone 31941.
SEQ ID NO: 433 is the determined cDNA sequence for clone 31982.
SEQ ID NO: 434 is the determined cDNA sequence for clone 31996.
20 SEQ ID NO: 435 is the determined cDNA sequence for clone 32010.
SEQ ID NO: 436 is the determined cDNA sequence for clone 31974.
SEQ ID NO: 437 is the determined cDNA sequence for clone 31983.
SEQ ID NO: 438 is the determined cDNA sequence for clone 31999.
SEQ ID NO: 439 is the determined cDNA sequence for clone 31949.
25 SEQ ID NO: 440 is the determined cDNA sequence for clone 31947.
SEQ ID NO: 441 is the determined cDNA sequence for clone 31994.
SEQ ID NO: 442 is the determined cDNA sequence for clone 31958.
SEQ ID NO: 443 is the determined cDNA sequence for clone 31975.
SEQ ID NO: 444 is the determined cDNA sequence for clone 31984.
30 SEQ ID NO: 445 is the determined cDNA sequence for clone 32024.
SEQ ID NO: 446 is the determined cDNA sequence for clone 31972.

SEQ ID NO: 447 is the determined cDNA sequence for clone 31943.
SEQ ID NO: 448 is the determined cDNA sequence for clone 32018.
SEQ ID NO: 449 is the determined cDNA sequence for clone 32026.
SEQ ID NO: 450 is the determined cDNA sequence for clone 32009.
5 SEQ ID NO: 451 is the determined cDNA sequence for clone 32019.
SEQ ID NO: 452 is the determined cDNA sequence for clone 32025.
SEQ ID NO: 453 is the determined cDNA sequence for clone 31967.
SEQ ID NO: 454 is the determined cDNA sequence for clone 31968.
SEQ ID NO: 455 is the determined cDNA sequence for clone 31955.
10 SEQ ID NO: 456 is the determined cDNA sequence for clone 31951.
SEQ ID NO: 457 is the determined cDNA sequence for clone 31970.
SEQ ID NO: 458 is the determined cDNA sequence for clone 31962.
SEQ ID NO: 459 is the determined cDNA sequence for clone 32001.
SEQ ID NO: 460 is the determined cDNA sequence for clone 31953.
15 SEQ ID NO: 461 is the determined cDNA sequence for clone 31944.
SEQ ID NO: 462 is the determined cDNA sequence for clone 31825.
SEQ ID NO: 463 is the determined cDNA sequence for clone 31828.
SEQ ID NO: 464 is the determined cDNA sequence for clone 31830.
SEQ ID NO: 465 is the determined cDNA sequence for clone 31841.
20 SEQ ID NO: 466 is the determined cDNA sequence for clone 31847.
SEQ ID NO: 467 is the determined cDNA sequence for clone 31850.
SEQ ID NO: 468 is the determined cDNA sequence for clone 31852.
SEQ ID NO: 469 is the determined cDNA sequence for clone 31855.
SEQ ID NO: 470 is the determined cDNA sequence for clone 31858.
25 SEQ ID NO: 471 is the determined cDNA sequence for clone 31861.
SEQ ID NO: 472 is the determined cDNA sequence for clone 31868.
SEQ ID NO: 473 is the determined cDNA sequence for clone 31870.
SEQ ID NO: 474 is the determined cDNA sequence for clone 31872.
SEQ ID NO: 475 is the determined cDNA sequence for clone 31873.
30 SEQ ID NO: 476 is the determined cDNA sequence for clone 31877.
SEQ ID NO: 477 is the determined cDNA sequence for clone 31878.

WO 00/37643

27

PCT/US99/30909

SEQ ID NO: 478 is the determined cDNA sequence for clone 31885.

SEQ ID NO: 479 is the determined cDNA sequence for clone 31888.

SEQ ID NO: 480 is the determined cDNA sequence for clone 31890.

SEQ ID NO: 481 is the determined cDNA sequence for clone 31893.

5 SEQ ID NO: 482 is the determined cDNA sequence for clone 31898.

SEQ ID NO: 483 is the determined cDNA sequence for clone 31901.

SEQ ID NO: 484 is the determined cDNA sequence for clone 31909.

SEQ ID NO: 485 is the determined cDNA sequence for clone 31910.

SEQ ID NO: 486 is the determined cDNA sequence for clone 31914.

10

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as colon cancer. The compositions described herein may include colon tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a colon tumor protein or a variant thereof. A "colon tumor protein" is a protein that is expressed in colon tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain colon tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with colon cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence.

15 20 25 Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

WO 00/37643

28

PCT/US99/30909

The present invention is based on the discovery of human colon tumor proteins. Sequences of polynucleotides encoding specific tumor proteins are provided in SEQ ID NO: 1-121, 123-197 and 205-486.

5 COLON TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a colon tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode
10 a portion of a colon tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a colon tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain
15 introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous
20 sequence that encodes a colon tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein.
25 Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native colon tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for
30 maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and

WO 00/37643

29

PCT/US99/30909

compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

5 Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of
10 Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenesis pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M.
15 (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing
20 two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is
25 calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

30 Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of

hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native colon tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C
5 for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to
10 differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles
15 may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two
20 fold greater in a colon tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA
25 prepared from cells expressing the proteins described herein, such as colon tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable
30 library (*e.g.*, a colon tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide

WO 00/37643

31

PCT/US99/30909

probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

5 For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using
10 standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full
20 length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about
25 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and
30 used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by

WO 00/37643

32

PCT/US99/30909

amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid
5 amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic. 1*:111-19, 1991) and walking PCR (Parker et al.,
10 *Nucl. Acids Res. 19*:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using
15 well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding portions of colon tumor proteins are provided in SEQ ID NO: 1-121, 123-197 and 205-486. These polynucleotides were isolated from colon tumor cDNA libraries using conventional and/or
20 PCR-based subtraction techniques, as described below.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see
25 Adelman et al., *DNA 2*:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a colon tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered
30 to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting

WO 00/37643

33

PCT/US99/30909

antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a colon tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into
5 cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of
10 polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In* Huber and Carr, *Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes. ...

15 A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30
20 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such
25 as inosine, queosine and wybutosine, as well as acetyl-, methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include
30 expression vectors, replication vectors, probe generation vectors and sequencing vectors. In

general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

COLON TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a colon tumor protein or a variant thereof, as described herein. As noted above, a "colon tumor protein" is a protein that is expressed by colon tumor cells. Proteins that are colon tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with colon cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or

heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a colon tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native colon tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native colon tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native colon tumor protein in one or more substitutions, deletions, additions and/or insertions, such

that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain non-conservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

WO 00/37643

37

PCT/US99/30909

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A

WO 00/37643

38

PCT/US99/30909

fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing
5 fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant
10 protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that
15 the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into
20 the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred
25 peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1
30 to about 50 amino acids in length. Linker sequences are not required when the first and

second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid

proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology 10:795-798, 1992*). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

5 In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95%
10 pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-
15 binding fragments thereof, that specifically bind to a colon tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a colon tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a colon tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules
20 such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3
25 L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as colon cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a colon tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the
30 disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies

WO 00/37643

41

PCT/US99/30909

this requirement, biological samples (e.g., blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the
5 disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA
10 molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of
15 monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification.
20 Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then
25 be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of
30 immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example,

WO 00/37643

42

PCT/US99/30909

from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a
5 nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide.
10 Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or
15 the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of
20 antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity
25 chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and
30 purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid.

WO 00/37643

43

PCT/US99/30909

Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction
5 between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an
10 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate
15 the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl
20 groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable
25 linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S.
30 Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a colon tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from

WO 00/37643

45

PCT/US99/30909

Nexell Therapeutics Inc., Irvine, CA . Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

5 T cells may be stimulated with a colon tumor polypeptide, polynucleotide encoding a colon tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a colon tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

10 T cells are considered to be specific for a colon tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a colon tumor polypeptide (100
20 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience
25 (Greene 1998)). T cells that have been activated in response to a colon tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Colon tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

30 For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a colon tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro*

WO 00/37643

46

PCT/US99/30909

or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a colon tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a colon tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a colon tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances or potentiates an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the

WO 00/37643

47

PCT/US99/30909

necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and

5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or
5 preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this
10 invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories,
15 Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12,
20 may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type
25 cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these
30 cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

WO 00/37643

49

PCT/US99/30909

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT) (*see* US Patent Nos. 5 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a 10 monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is 15 described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of 20 polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within 25 a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be 30 treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical

WO 00/37643

50

PCT/US99/30909

compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

APCs may generally be transfected with a polynucleotide encoding a colon tumor protein (or portion or other variant thereof) such that the colon tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the colon tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as colon cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a “patient” refers to any warm-blooded animal, preferably a human. A patient may or

may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may
5 be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as
10 polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells
15 include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and
20 transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding
25 single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient
30 number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive

WO 00/37643

53

PCT/US99/30909

polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient,

WO 00/37643

54

PCT/US99/30909

but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a colon tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more colon tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as colon cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a colon tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of

WO 00/37643

55

PCT/US99/30909

the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length colon tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with colon cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

5 The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting
10 the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the
15 addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as colon cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred
20 embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to
25 the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value
30 that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered

positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

5 In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent
10 flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of
15 immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to
20 generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

25 Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use colon tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such
30 colon tumor protein specific antibodies may correlate with the presence of a cancer.

WO 00/37643

59

PCT/US99/30909

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a colon tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a colon tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with one or more representative polypeptides (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of colon tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a colon tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a colon tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the colon tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a colon tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a colon tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will

WO 00/37643

60

PCT/US99/30909

hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-121, 123-197 and 205-486. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may

WO 00/37643

61

PCT/US99/30909

also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple colon tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a colon tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a colon tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a colon tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a colon tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

5

Example 1

ISOLATION AND CHARACTERIZATION OF COLON TUMOR POLYPEPTIDES BY
PCR-BASED SUBTRACTION AND MICROARRAY ANALYSIS

A cDNA library was constructed in the PCR2.1 vector (Invitrogen, Carlsbad,
10 CA) by subtracting a pool of three colon tumors with a pool of normal colon, spleen, brain,
liver, kidney, lung, stomach and small intestine using PCR subtraction methodologies
(Clontech, Palo Alto, CA). The subtraction was performed using a PCR-based protocol,
which was modified to generate larger fragments. Within this protocol, tester and driver
double stranded cDNA were separately digested with five restriction enzymes that recognize
15 six-nucleotide restriction sites (MluI, MscI, PvuII, Sall and StuI). This digestion resulted in
an average cDNA size of 600 bp, rather than the average size of 300 bp that results from
digestion with RsaI according to the Clontech protocol. This modification did not affect the
subtraction efficiency. Two tester populations were then created with different adapters, and
the driver library remained without adapters.

20 The tester and driver libraries were then hybridized using excess driver cDNA.
In the first hybridization step, driver was separately hybridized with each of the two tester
cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester
cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs, and
(d) unhybridized driver cDNAs. The two separate hybridization reactions were then
25 combined, and rehybridized in the presence of additional denatured driver cDNA. Following
this second hybridization, in addition to populations (a) through (d), a fifth population (e) was
generated in which tester cDNA with one adapter hybridized to tester cDNA with the second
adapter. Accordingly, the second hybridization step resulted in enrichment of differentially
expressed sequences which could be used as templates for PCR amplification with adaptor-
30 specific primers.

The ends were then filled in, and PCR amplification was performed using
adaptor-specific primers. Only population (e), which contained tester cDNA that did not

WO 00/37643

63

PCT/US99/30909

hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed
5 cDNAs so that rare transcripts that are over-expressed in colon tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

To characterize the complexity and redundancy of the subtracted library, 96 clones were randomly picked and 65 were sequenced, as previously described. These
10 sequences were further characterized by comparison with the most recent Genbank database (April, 1998) to determine their degree of novelty. No significant homologies were found to 21 of these clones, hereinafter referred to as 11092, 11093, 11096, 11098, 11103, 11174, 11108, 11112, 11115, 11117, 11118, 11134, 11151, 11154, 11158, 11168, 11172, 11175, 11184, 11185 and 11187. The determined cDNA sequences for these clones are provided in
15 SEQ ID NO: 48, 49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101 and 109-111, respectively.

Two-thousand clones from the above mentioned cDNA subtraction library were randomly picked and submitted to a round of PCR amplification. Briefly, 0.5 µl of glycerol stock solution was added to 99.5 µl of pcr MIX (80 µl H₂O, 10 µl 10X PCR Buffer, 6 µl 25 mM MgCl₂, 1 µl 10 mM dNTPs, 1 µl 100 mM M13 forward primer
20 (CACGACGTTGTAAAACGACGG), 1 µl 100 mM M13 reverse primer (CACAGGAAACAGCTATGACC)), and 0.5 µl 5 u/ml Taq polymerase (primers provided by (Operon Technologies, Alameda, CA). The PCR amplification was run for thirty cycles under the following conditions: 95°C for 5 min., 92°C for 30 sec., 57°C for 40 sec., 75°C for 2 min. and 75°C for 5 minutes.

25 mRNA expression levels for representative clones were determined using microarray technology (Synteni, Palo Alto, CA) in colon tumor tissues (n=25), normal colon tissues (n=6), kidney, lung, liver, brain, heart, esophagus, small intestine, stomach, pancreas, adrenal gland, salivary gland, resting PBMC, activated PBMC, bone marrow, dendritic cells, spinal cord, blood vessels, skeletal muscle, skin, breast and fetal tissues. The number of
30 tissue samples tested in each case was one (n=1), except where specifically noted above; additionally, all the above-mentioned tissues were derived from humans. The PCR

amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, and fluorescent-labeled cDNA probes were generated by reverse transcription according to the protocol provided by Synteni. The microarrays were probed with the labeled
5 cDNA probes, the slides scanned, and fluorescence intensity was measured. This intensity correlates with the hybridization intensity.

One hundred and forty nine clones showed two or more fold over-expression in the colon tumor probe group as compared to the normal tissue probe group. These cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied
10 Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). These sequences were compared to known sequences in the most recent GenBank database. No significant homologies to human gene sequences were found in forty nine of these clones, represented by the following sixteen cDNA consensus sequences: SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46 and 47, hereinafter referred to as Contig 2, 8,
15 13, 14, 20, 23, 29, 31, 35, 32, 36, 38, 41, 42, 50 and 51, respectively). Contig 29 (SEQ ID NO: 30) was found to be a Rat GSK-3- β -interacting protein Axil homolog. Also, Contigs 31 and 35 (SEQ ID NO: 32 and 33, respectively) were found to be a Mus musculus GOB-4 homolog. The determined cDNA sequences of SEQ ID NO: 1, 3-7, 9-14, 17-21, 23, 25-29, 31, 35, 37, 39, 42-45, 50, 51, 53, 55-58, 61-64, 70-78, 80-88, 91, 92, 94-98, 102-108 and 112
20 were found to show some homology to previously identified genes sequences.

Microarray analysis demonstrated Contig 2 (SEQ ID NO: 2) showed over-expression in 34% of colon tumors tested, as well as increased expression in normal pancreatic tissue, with no over-expression in normal colon tissues. Upon further analysis, Contigs 2, 8 and 23 were found to share homology to the known gene GW112. Contigs 4, 5,
25 9 and 52 showed homology to carcinoembryonic antigen (SEQ ID NO: 3, 4, 5 and 6, respectively). A representative sampling of these fragments showed over-expression in 85% of colon tumors, with over-expression in normal bone marrow and 3/6 normal colon tissues. Contig 6 (SEQ ID NO: 7), showing homology to the known gene sequence for villin, and was over-expressed in about half of all colon tumors tested, with a limited degree of low level
30 over-expression in normal colon. Contig 12 (SEQ ID NO: 14), showing homology to Chromosome 17, clone hRPC.1171_I_10, also referred to as C798P, was over-expressed in

WO 00/37643

65

PCT/US99/30909

approximately 70% of colon tumors tested, with low over-expression in 1/6 normal colon samples. Contig 14, also referred to as 14261 (SEQ ID NO: 16), showing no significant homology to any known gene, showed over-expression in 44% of colon tumors tested, with low level expression in half of normal colon tissues, as well as small intestine and pancreatic tissue. Contig 18 (SEQ ID NO: 21), showing homology to the known gene for L1-cadherin, showed over-expression in approximately half of colon tumors and low level over-expression in 3/6 normal colon tissues tested. Contig 22 (SEQ ID NO: 23), showing homology to Bumetanide-sensitive Na-K-Cl cotransporter was over-expressed in 70% of colon tumors and no over-expression in all normal tissues tested. Contig 25 (SEQ ID NO: 25), showing homology to macrophage inflammatory protein-3 α , was over-expressed in over 40% of colon tumors and in activated PBMC. Contigs 26 and 48 (SEQ ID NOS: 25 and 26), showing homology to the sequence for laminin, was over-expressed in 48% of colon tumors and with low over-expression in stomach tissue. Contig 28 (SEQ ID NO: 29), showing homology to the known gene sequence for Chromosome 16 BAC clone CIT987SK-A-363E6, was over-expressed in 33% of colon tumors tested with normal stomach and 2/6 normal colon tissues showing low level over-expression. Contigs 29, 31 and 35 (SEQ ID NOS: 30, 32 and 33, respectively), also referred to as C751P, an unknown sequence showing limited and partial homology to Rat GSK-3 β -interacting protein Axil homolog and Mus musculus GOB-4 homolog, was over-expressed in 74% of colon tumors and no over-expression in all normal tissues tested. Contig 34 (SEQ ID NO: 35), showing homology to the known sequence for desmoglein 2, was over-expressed in 56% of colon tumors and showed low level over-expression in 1/6 normal colon tissues. Contig 36 (SEQ ID NO: 36), an unknown sequence also referred to as C793P, showed over-expression in 30% of colon tumor tissues tested. Contig 37 and 14287.2 (SEQ ID NOS: 37 and 116), an unknown sequence, but with limited (89%) homology to the known sequence for putative transmembrane protein was over-expressed in 70% of colon tumors, as well as in normal lung tissue and 3/6 normal colon tissues tested. Contig 38, also referred to as C796P and 14219 (SEQ ID NO: 38), showing no significant homology to any known gene, was over-expressed in 38% in colon tumors and no elevated over-expression in any normal tissues. Contig 41 (SEQ ID NO: 40), also referred to as C799P and 14308, an unknown sequence showing no significant homology to any known gene, was over-expressed in 22% of colon tumors. Contig 42, (SEQ ID NO: 41), also

referred to as C794P and 14309, an unknown sequence with no significant homology to any known gene, was over-expressed in 63% of colon tumors tested, as well as in 3/6 normal colon tissues. Contig 43 (SEQ ID NO: 42), showing homology to the known sequence for Chromosome 1 specific transcript KIAA0487 was over-expressed in 85% of colon tumors tested and in normal lung and 4/6 normal colon tissues. Contig 49 (SEQ ID NO: 45), showing homology to the known sequence for pump-1, was over-expressed in 44% of colon tumors and no over-expression in all normal tissues tested. Contig 50 (SEQ ID NO: 46), also referred to as C792P and 18323, showing no significant homology to any known gene, was over-expressed in 33% of colon tumors with no detectable over-expression in any normal tissues tested. Contig 51 (SEQ ID NO: 47), also referred to as C795P and 14317 was over-expressed in 11% of colon tumors.

Additional microarray analysis yielded seven clones showing two or more fold over-expression in the colon tumor probe group as compared to the normal tissue probe group. Three of these clones demonstrated particularly good colon tumor specificity, and are represented by SEQ ID NO: 115, 116 and 120. Specifically, SEQ ID NO: 115, referred to as C791P or 14235, which shows homology to the known gene sequence for H. sapiens chromosome 21 derived BAC containing ets-2 gene, was over-expressed in 89% of colon tumors tested and in 5/6 normal colon tissues, as well as over-expressed at low levels in normal lung and activated PBMC. Microarray analysis for SEQ ID NO: 116 is discussed above. SEQ ID NO: 120, referred to as 14295, showing homology to the known gene sequence for secreted cement gland protein XAG-2 homolog, was over-expressed in 70% of colon tumors and in 5/6 normal colon tissues, as well as low level over-expression in normal small intestine, stomach and lung. All clones showing over-expression in colon tumor were sequenced and these sequences compared to the most recent Genbank database (February 12, 1999). Of the seven clones, three contained sequences that did not share significant homology to any known gene sequences, represented by SEQ ID NO: 116, 117 and 119. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in colon. The determined cDNA sequences of the remaining clones (SEQ ID NO: 113-115 and 120) were found to show some homology to previously identified genes.

Further analysis identified a clone which was recovered several times by PCR subtraction and by expression screening using a mouse anti-scld antiserum. The determined

WO 00/37643

67

PCT/US99/30909

full length cDNA sequence for this clone is provided in SEQ ID NO: 121, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 122. This clone is homologous with the known gene Beta IG-H3, as disclosed in U.S. Patent No. 5,444,164. Microarray analysis demonstrated this clone to be over-expressed in 75 to 80% of colon tumors tested (n=27), with no over-expression in normal colon samples (n=6), but with some low level over-expression in other normal tissues tested.

Further analysis of the PCR-subtraction library described above led to the isolation of longer cDNA sequences for the clones of SEQ ID NO: 30, 115, 46, 118, 41, 47, 38, 113, 14 and 40 (known as C751P, C791P, C792P, C793P, C794P, C795P, C796P, C797P, C798P and C799P, respectively). These determined cDNA sequences are provided in SEQ ID NO: 123-132, respectively.

Using PCR subtraction methodology described above with minor modifications, transcripts from a pool of three moderately differentiated colon adenocarcinoma samples were subtracted with a set of transcripts from normal brain, pancreas, bone marrow, liver, heart, lung, stomach and small intestine. Modifications of the above protocol were included at the cDNA digestion steps and in the tester to drive hybridization ratios. In a first subtraction, the restriction enzymes PvuII, DraI, MscI and StuI were used to digest cDNAs, and the tester to driver ratio was 1:40, as suggested by Clontech. In a second subtraction, DraI, MscI and StuI were used for cDNA digestion and a tester to driver ratio of 1:76 was used. Following the PCR amplification steps, the cDNAs were clones into pCR2.1 plasmid vector. The determined cDNA sequences of 167 isolated clones are provided in SEQ ID NO: 205-371. These sequences were compared to sequences in the public databases as described above. The sequences of SEQ ID NO: 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369 and 371 were found to show some homology to previously identified ESTs. The remaining sequences were found to show some homology to previously identified genes.

Using the PCR subtraction technology described above, a cDNA library from a pool of primary colon tumors was subtracted with a cDNA library prepared from normal tissues, including brain, bone marrow, kidney, heart, lung, liver, pancreas, small intestine,

WO 00/37643

68

PCT/US99/30909

stomach and trachea. The determined cDNA sequences for 90 clones isolated in this subtraction are provided in SEQ ID NO: 372-461. Comparison of these sequences with those in the public databases as described above, revealed no homologies to the sequences of SEQ ID NO: 426, 445 and 453. The sequences of SEQ ID NO: 372-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455 and 457-461 showed some homology to previously identified genes, while the sequences of SEQ ID NO: 379, 405, 407, 408, 418, 424, 430-432, 437, 442, 444, 452 and 456 showed some homology to previously isolated ESTs.

Example 2

ISOLATION OF TUMOR POLYPEPTIDES USING SCID-PASSAGED TUMOR RNA

Human colon tumor antigens were obtained using SCID mouse passaged colon tumor RNA as follows. Human colon tumor was implanted in SCID mice and harvested, as described in Patent Application Serial No. 08/556,659 filed 11/13/95, U.S. Patent No. 5,986,170 . First strand cDNA was synthesized from poly A+ RNA from three SCID mouse-passaged colon tumors using a Lambda ZAP Express cDNA synthesis kit (Stratagene). The reactions were pooled and digested with RNase A, T1 and H to cleave the RNA and then treated with NaOH to degrade the RNA. The resulting cDNA was annealed with biotinylated (Vector Labs, Inc., Burlingame, CA) cDNA from a normal resting PBMC plasmid library (constructed from Superscript plasmid System, Gibco BRL), and subtracted with streptavidin by phenol/chloroform extraction. Second strand cDNA was synthesized from the subtracted first strand cDNA and digested with S1 nuclease (Gibco BRL). The cDNA was blunted with Pfu polymerase and EcoRI adaptors (Stratagene) were ligated to the ends. The cDNA was phosphorylated with T4 polynucleotide kinase, digested with restriction endonuclease XhoI, and size selected with Sephacryl S-400 (Sigma). Fractions were pooled, ligated to Lambda ZAP Express arms (Stratagene) and packaged with Gigapack Gold III extract (Stratagene). Random plaques were picked, phagemid was excised, transformed into XL0LR cells (Stratagene) and resulting plasmid DNA (Qiagen Inc., Valencia, CA) was sequenced as described above. The determined cDNA sequences for 17

WO 00/37643

69

PCT/US99/30909

clones isolated as described above are provided in SEQ ID NO: 133-151, wherein 133 and 134 represent partial sequences of a clone referred to as CoSub-3 and SEQ ID NO: 135 and 136 represent partial sequences of a clone referred to as CoSub-13. These sequences were compared with those in the public databases as described above. The sequences of SEQ ID NO: 139 and 149 showed no significant homologies to any previously identified sequences. The sequences of SEQ ID NO: 138, 140, 141, 142, 143, 148 and 149 showed some homology to previously isolated expressed sequence tags (ESTs). The sequences of SEQ ID NO: 133-137, 144-147, 150 and 151 showed some homology to previously isolated gene sequences.

10

Example 3

USE OF MOUSE ANTISERA TO IDENTIFY DNA SEQUENCES ENCODING COLON TUMOR ANTIGENS

This example illustrates the isolation of cDNA sequences encoding colon tumor antigens by screening of colon tumor cDNA libraries with mouse anti-tumor sera.

A cDNA expression library was prepared from SCID mouse-passaged human colon tumor poly A+ RNA using a Stratagene (La Jolla, CA) Lambda ZAP Express kit, following the manufacturer's instructions. Sera was obtained from the colon tumor-bearing SCID mouse. This serum was injected into normal mice to produce anti-colon tumor serum. Approximately 600,000 PFUs were screened from the unamplified library using this antiserum. Using a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (BRL Labs.), positive plaques were identified. Phage was purified and phagemid excised for several clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

The determined cDNA sequences for 46 of the isolated clones are provided in SEQ ID NO: 152-197. The predicted amino acid sequences for the cDNA sequences of SEQ ID NO: 187, 188, 189, 190, 194, 195 and 197 are provided in SEQ ID NO: 198-204, respectively. The determined cDNA sequences were compared with those in the public database as described above. The sequences of SEQ ID NO: 156, 168, 184, 189, 192 and 196 showed some homology to previously isolated ESTs. The sequences of SEQ ID NO: 152-

30

155, 157-167, 169-182, 183, 185-188, 190, 194, 195 and 197 showed some homology to previously identified genes.

Example 4

5 ISOLATION AND CHARACTERIZATION OF COLON TUMOR POLYPEPTIDES BY CONVENTIONAL SUBTRACTION

Two cDNA libraries were constructed and used to create a subtracted cDNA library as follows.

10 Using the GibcoBRL Superscript Plasmid System with minor modifications, two cDNA libraries were created. The first library, referred to as CTCL, was prepared from a pool of mRNA samples from three colon adenocarcinoma tissue samples. Two of the samples were described as Duke's stage C and one as Duke's stage B. All three samples were grade III in histological status. A second library (referred to as DriverLibpcDNA3.1+)
15 was prepared from a pool of normal tissues, namely liver, pancreas, skin, bone marrow, resting PBMC, stomach and brain. Both libraries were prepared using the manufacturer's instructions with the following modifications: an EcoRI-NotI 5' cDNA adapter was used instead of the provided reagent; the vector pCDNA3.1(+) (Invitrogen) was substituted for the pSPORT vector; and the ligated DNA molecules were transformed into ElectroMaxDH10B
20 electrocompetent cells. Clones from the libraries were analyzed by restriction digest and sequencing to determine average insert size, quality of the library and complexity of the library. DNA was prepared from each library and digested.

The driver DNA was biotinylated and hybridized with the colon library tester DNA at a ratio of 10:1. After two rounds of hybridizations, streptavidin incubations and
25 extractions, the remaining colon cDNAs were size-selected by column chromatography and cloned into the pCMV-Script vector from Stratagene. Clones from this subtracted library (referred to as CTCL-S1) were characterized as described above for the unsubtracted libraries.

The determined cDNA sequences for 18 clones isolated from the CTCL-S1 library are provided in SEQ ID NO: 462-479. Comparison of these sequences with those in
30 the public databases, as described above, revealed no significant homologies to the sequences

WO 00/37643

71

PCT/US99/30909

of SEQ ID NO: 476, 477 and 479. The remaining sequences showed some homology to previously identified genes.

In further studies, a cDNA library was prepared from a pool of mRNA from three metastatic colon adenocarcinomas derived from liver tissue samples. All samples were
5 described as Duke's stage D. Conventional subtraction was performed as described above, using the DriverLibpcDNA3.1+ library described above as the driver. The resulting subtracted library (referred to as CMCL-S1) was characterized by isolating a set of clones for restriction analysis and sequencing.

The determined cDNA sequences for 7 clones isolated from the CMCL-S1
10 library are provided in SEQ ID NO: 480-486. Comparison of these sequences with those in the public databases revealed no significant homologies to the sequence of SEQ ID NO: 483. The sequences of SEQ ID NO: 480-482 and 484-486 were found to show some homology to previously identified genes.

15

Example 5

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-
20 N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the
25 peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or
30 other types of mass spectrometry and by amino acid analysis.

WO 00/37643**72****PCT/US99/30909**

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

WO 00/37643

73

PCT/US99/30909

CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a colon tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483;

(b) sequences that hybridize to a sequence of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 under moderately stringent conditions; and

(c) a complement of a sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168,

WO 00/37643

74

PCT/US99/30909

170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 5 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 122 and 198-204.

10 4. An isolated polynucleotide encoding at least 15 amino acid residues of a colon tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of
15 SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356,
20 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a colon tumor protein, or a variant
25 thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253,
30 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303,

WO 00/37643

75

PCT/US99/30909

310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 or a complement of any of the foregoing sequences.

5 6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279,
10 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483.

 7. An isolated polynucleotide comprising a sequence that hybridizes to a
15 sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303, 310-313, 315, 317, 320,
20 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455, 457-461, 476, 477, 479 and 483 under moderately stringent conditions.

 8. An isolated polynucleotide complementary to a polynucleotide
25 according to any one of claims 4-7.

 9. An expression vector comprising a polynucleotide according to any one of claims claim 4-8.

30 10. A host cell transformed or transfected with an expression vector according to claim 9.

30 17. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

WO 00/37643

77

PCT/US99/30909

- 5 (a) a polypeptide according to claim 1;
(b) a polynucleotide according to claim 4;
(c) an antibody according to claim 11;
(d) a fusion protein according to claim 12; and
(e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 10 (a) a polypeptide according to claim 1;
(b) a polynucleotide according to claim 4;
(c) an antibody according to claim 11;
(d) a fusion protein according to claim 12; and
(e) a polynucleotide according to claim 16.

15 19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20 20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

25 22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

30 23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

WO 00/37643

78

PCT/US99/30909

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.

26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486, and thereby inhibiting the development of a cancer in the patient.

30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is colon cancer.

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-121, 123-

WO 00/37643

79

PCT/US99/30909

197 and 205-486; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

5

33. A method according to claim 32, wherein the biological sample is blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient,
10 comprising administering to a patient a biological sample treated according to the method of claim 50.

35. A method for stimulating and/or expanding T cells specific for a colon tumor protein, comprising contacting T cells with at least one component selected from the
15 group consisting of:

- (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-121, 123-197 and 205-486;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
- 20 (iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii),
under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

36. An isolated T cell population, comprising T cells prepared according to
25 the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

30

38. A method for inhibiting the development of a cancer in a patient,

comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

- (i) a polypeptide according to claim 1;
- 5 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-121, 123-197 and 205-486;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
- (iv) an antigen-presenting cell that expresses a polypeptide of (i) or
- 10 (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

15 39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with at least one component selected from the group consisting of:

- (i) a polypeptide according to claim 1;
- 20 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-121, 123-197 and 205-486;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and
- (iii) an antigen-presenting cell that expresses a polypeptide of (i) or
- 25 (ii);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

(c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

30

40. A method for determining the presence or absence of a cancer in a

WO 00/37643

81

PCT/US99/30909

patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

5 (i) polynucleotides recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

10 (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

41. A method according to claim 40, wherein the binding agent is an antibody.

15

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

43. A method according to claim 40, wherein the cancer is colon cancer.

20

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in
25 any one of SEQ ID NO: 1-121, 123-197 and 205-486 or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

30

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

WO 00/37643

82

PCT/US99/30909

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

47. A method according to claim 44, wherein the cancer is a colon cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486 or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

30

51. A method for monitoring the progression of a cancer in a patient,

WO 00/37643

83

PCT/US99/30909

comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a colon tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1-121, 123-197 and 205-486 or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

- (a) one or more antibodies according to claim 11; and
- (b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

57. A kit according to claim 54, wherein the reporter group is selected

WO 00/37643

84

PCT/US99/30909

from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that
5 hybridize under moderately stringent conditions to a polynucleotide that encodes a colon
tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded
by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 8, 15, 16, 22, 24, 30, 32-
34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111, 116-119,
123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205, 207, 210-
10 212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250, 253, 254,
256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302, 303,
310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-378,
380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454, 455,
457-461, 476, 477, 479 and 483 or a complement of any of the foregoing polynucleotides.

15

59. A oligonucleotide according to claim 58, wherein the oligonucleotide
comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 2, 8, 15, 16, 22,
24, 30, 32-34, 36, 38, 40, 41, 46-49, 52, 54, 59, 60, 65-69, 79, 89, 90, 93, 99-101, 109-111,
116-119, 123-132, 138-142, 143, 148, 149, 156, 168, 170-182, 184, 189, 191-193, 196, 205,
20 207, 210-212, 214, 215, 218, 224-226, 228, 233, 234, 236, 238, 241, 242, 245, 246, 248, 250,
253, 254, 256, 259, 260, 262, 263, 266, 267, 270-273, 279, 282, 291, 293, 294, 298, 300, 302,
303, 310-313, 315, 317, 320, 322, 324, 332-335, 345, 347, 356, 358, 361, 362, 366, 369, 371-
378, 380-404, 406, 409-417, 419-423, 425, 427-429, 433-436, 438-441, 443, 446-451, 454,
455, 457-461, 476, 477, 479 and 483.

25

60. A diagnostic kit, comprising:

(a) an oligonucleotide according to claim 59; and

(b) a diagnostic reagent for use in a polymerase chain reaction or
hybridization assay.

WO 00/37643

PCT/US99/30909

1

SEQUENCE LISTING

<110> Corixa Corporation

<120> COMPOUNDS FOR IMMUNOTHERAPY AND
DIAGNOSIS OF COLON CANCER AND METHODS FOR THEIR USE

<130> 210121.471PC

<140> PCT

<141> 1999-12-23

<160> 486

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 458

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(458)

<223> n = A,T,C or G

<400> 1

ncagggtctgg	cggcacctgt	gcactcagcc	gtcgatcac	tggtcgattg	ggacagggaa	60
gacgatgtgg	ttttcagggg	ggcccagaga	tttggagaag	cggatgaagt	tctcctttag	120
ttccgaagtc	agctccttgg	ttctcccgta	gaggggtgatc	ttgaagtaac	ccctgttttg	180
agaaactttc	ttgaagaaca	ccatagcatg	ctggttgtag	ttggtgctca	ccactcggac	240
gaggtaactc	gttaatccag	ggtaactctt	aatggttgccc	agcgtgaact	cgccgggctg	300
gcaacctgga	acaaaagtcc	tgatccagta	gtcacacttc	tttttcttaa	acaggacgga	360
ggtgacattg	tagctcttgt	cttcttttcag	ctcatagatg	gtggcataca	tcttttgctg	420
gtctttgtct	tctctgagaa	ttgcattccc	tgccagga			458

<210> 2

<211> 423

<212> DNA

<213> Homo sapien

<400> 2

cagggtccat	aggtgatccg	caactctcga	gcattttatat	acaatagcaa	atcatccagt	60
gtgttgtaca	gtctataata	ctccaacagt	ctcccatctg	tattcaatgg	cgccacccaa	120
tacagtcctt	tggttgatg	ctggggagag	taatccctac	cccaagcacc	atatagataa	180
gaaaaccctc	tccagttgag	ctgaaccaca	gacgggtttgc	tgatgttcac	cacaccacca	240
tgaccacagc	tccctggagt	gggaggaggg	tgacgacag	gggtgttttg	atcttttagag	300
gcttcacact	ctttcagctt	ggtcttcaga	gccacgattt	ctcggcgaat	ggcaaggaca	360
ttgtttttgt	ctagtgtctc	aagcttctct	accaagagag	tcatttttct	tatctccacc	420
tcc						423

<210> 3

<211> 538

WO 00/37643

PCT/US99/30909

3

<211> 401
 <212> DNA
 <213> Homo sapien

<400> 7
 tgggtgttgtt ggccgaggt ccttgacgt ggaacagccg tgtggagggc ccggtctcca 60
 agttgttagt tcgggaggtg cctccctggt agaccaccat gcgtcccttg aagatggaca 120
 taagatgagg tggctccttg cccattggga cccggatctg gactgggtca ccattgtact 180
 tctggtccag gatgacggct tgataagctg atgctgtaat ttcatcttgg ctggcctggc 240
 tgccctgcc aacgtagagc aggtaatgct gcttctcgcc gatgaaggta ggtgtaagag 300
 cagcaggtaa gcaagttcgc ccccatagaa gtgggcctag ccacttgga ttccagcaca 360
 ctggcggccc gttactagtg ggatcccag ctcggtacca a 401

<210> 8
 <211> 1151
 <212> DNA
 <213> Homo sapien

<400> 8
 ctctctccat aaaactcagc actttacaga tgtagaatat ataagcatgc caaatctact 60
 tatctgccac atacaaagca tcattccagg tgctagttag gggaaaaaaa agttggagat 120
 ttggctccctc gaggagctcc agatattaat ctacctaact aagtcgccag gttctctcca 180
 ggcattggaag aattagtggc gctacatgga tgaggactag tcattgggca atatttctctg 240
 tacaaagaat ccttagacgc catactgagt tttaagttcc ttaatttcta atttaaggct 300
 tctagtgaag cctctcaca gtaggcttca ctaggccac agtccccca gacctctgac 360
 aatccccccc tagacagact ttattgcaaa atgcgcctga agaggcagat gatccccag 420
 agaactcacc aaatcaagac aaatgtccta gatctcragt gtggtagaac tatgcacct 480
 aacattgctg caaaatgaac acacttttag acaccctgc agatatctaa gtaagtggag 540
 aagactatct tttcaacaaa cattttctct ttcacctaa ctctaaaca gcttactggg 600
 gcttctgcaa gacagaaaga tcataattca gaaggtaacc atcgctatag acataaagtt 660
 tctggtcaaa agggttatag ttaatgctct gcacttttct ctgcatctta tgcattacaa 720
 tgtctagttt gccctcttct cctgtgtttg tgcataata gtaaaaaatc tcttctgttc 780
 tgggtgtttca tagtacgggt ggcatacaga accccacata ccatgaaggc gttagaagca 840
 gatggtttat actgcttggc ataccaagtg tttagcacct gaagtgtggt gtcatttagt 900
 ttactaatca ccatgttacc agtgctggct tcagttgaat aaataaccca caatccattc 960
 tcatccacag caaagtcaat atcttgccaa gcaacattag catatgaaaa gcggttatta 1020
 taggcagcat tagggagagt ttgagtcaca gcaatcgtgt tggtygtcag gtttaactctg 1080
 gcaatattcc cgggtgtgta catgttgacg tacatgttgt tgttgtaaac tgctgtacca 1140
 ctacctgga c 1151

<210> 9
 <211> 604
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(604)
 <223> n = A,T,C or G

<400> 9
 ctgtgcaagg gctttacaaa aactgtgcca ggacttccca tgaggctgga ttgcttgatt 60
 catgttttat gagccccaca atactgaagc tccttttcca gggacttggc ataggcagtc 120
 aattccacat ttgggatagg tcctctcttg aagtgaatgt caggcagtga catccaagtt 180
 tctgcatgca gtgggttaac agccatgttt agggggaaca tgatttaaaa agtacatctc 240

WO 00/37643

PCT/US99/30909

4

```
tctccctcct cccccacatg cacaaggctc acatctcatt atgggtgkcg cccatgtcac 300
attaaagtgt gatacttkgg ttttgaaaac attcaaacag tctctgtgga aatctggaga 360
gaaattggcg gagagctgcc gtggtgcatt cctcctgtag tgcttcaagn taatgcttca 420
tcctttntta ataacttttg atagacaggg gctagtcgca cagacctctg ggaagccctg 480
gaaaacgctg atgcttgttt gaagatctca agcgcagagt ctgcaagttc atccccctctt 540
tcctgaggtc tgttggtctgg aggctgcaga acattggtga tgacatggac cacgccattt 600
gtgg 604
```

<210> 10

<211> 473

<212> DNA

<213> Homo sapien

<400> 10

```
tcgagaagat ccctagttag actttgaacc gtatcctggg cgacccagaa gccctgagag 60
acctgctgaa caaccacatc ttgaagtcag ctatgtgtgc tgaagccatc gttgcggggc 120
tgtctgtgga gaccctggag ggcacgacac tggaggtggg ctgcagcggg gacatgctca 180
ctatcaacgg gaaggcgatc atctccaata aagacatcct agccaccaac ggggtgatcc 240
actacattga tgagctactc atcccagact cagccaagac actatttgaa ttggtgcag 300
agtctgatgt gtccacagcc attgaccttt tcagacaagc cggcctcggc aatcatctct 360
ctggaagtga gcggttgacc ctctgggct cccctgaatt ctgtattcaa agatggaacc 420
cctccaattg atgcccatac aaggaatttg cttcggaacc acataattaa aga 473
```

<210> 11

<211> 411

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(411)

<223> n = A,T,C or G

<400> 11

```
tcctcattgg tcggggccaa aagcgtgtac tggccgttac cttcaagcat cgtgttgagc 60
cctgatgcag ccacagcagc ccgaagggtc tcaaagggtg cctcgatctc aatgatctgc 120
tggatgttgt tggatgttgt ggagatgacc ttatcgatga ggtgcaccac cccgttgggt 180
gcatgggtgt cggttttyar carccgggca cagttcacag ttacaatccc attagatag 240
tggatggatct nggatgttgg aattctggta catagnaggt gaggggtcat gccgtgttt 300
cagctcatca gtcaggactc gcctgccac catatggtaa gcsgragggc atttgagcag 360
ctcaatgttt gacattgctg gaccagggga gttccagcac ttctangang a 411
```

<210> 12

<211> 560

<212> DNA

<213> Homo sapien

<400> 12

```
tacttgccctg gagatwgcyt tykckwtmtg ytcwrawgtc cgtggataca gaaatctctg 60
caggcaagtt gctccagagc atattgcagg acaagcctgt aacgaatagt taaattcacg 120
gcatctggat tcctaatect tttccgaaat ggcagggtgt agtgccctgta taaaatattc 180
tatgtttacc ttcaacttct tgttctggct atgtggtatc ttgatcctag cattagcaat 240
atgggtacga gtaagcaatg actctcaagc aatttttggg tctgaagatg taggctctag 300
ctcctacgtt gctgtggaca tattgattgc tgtaggtgcc atcatcatga ttctgggctt 360
cctgggatgc tgcggtgcta taaaagaaag tcgctgcatg cttctgttgt ttttcatagg 420
```

WO 00/37643

PCT/US99/30909

5

```

cttgcttctg atcctgctcc tgcaggtggg cgacaggtat cctaggagct gttttcaa
ctaagtctga tgcattgtg aatgaaactc tctatgaaaa cacaaagctt ttgagcgcca
caggggaaag tgaaaaacaa

```

480
540
560

```

<210> 13
<211> 150
<212> DNA
<213> Homo sapien

```

```

<400> 13
gggcaggctg tctttttaa atgtctcggc tagctagacc acagatatct tctagacata
ttgaacacat ttaagatttg agggatataa gggaaatga tatgaatgtg tatttttact
caaaataaaa gtaactgttt acgttgggtga

```

60
120
150

```

<210> 14
<211> 403
<212> DNA
<213> Homo sapien

```

```

<400> 14
ctgctgcctg tggcgtgtgt gggctggatc ccttgaaggc tgagtttttg agggcagaaa
gctagctatg ggtagccagg tgttaciaag gtgctgctcc ttctccaacc cctacttggg
ttccctcacc ccaagcctca tgttcatacc agccagtggg ttcagcagaa cgcattgacac
cttatcacct ccttccttgg gtgagctctg aacaccagct ttggcccctc cacagtaagg
ctgctacatc aggggcaacc ctggctctat catttttcct ttttgccaaa aggaccagta
gcataggtga gccctgagca ctaaaaggag gggtccttga agctttccca ctatagtgtg
gagttctgtc cctgaggtgg gtacagcagc cttgggttct ctg

```

60
120
180
240
300
360
403

```

<210> 15
<211> 688
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (688)
<223> n = A,T,C or G

```

```

<400> 15
caaagcacat tttaatcatt tattttaaaa gggggagtaa agcattttaa ctgccaatcc
tatagactag gacttgaaca tcaaaggaaa aatagacraa gactagatga taaagtcatt
caaaagcaca gaagcacatc acatacacca gcaaggtttc caactactgc actgattaac
tagatactct caatagcttt tctatagctc gtccatagaaa aaaaaattaa attttcattt
tcttacaagt tccaggctta aacaaaaggca aaaattacat gcaacaactg atacactcat
aagttgcaca tatgctccaa ggtctttatt agataacaat aaatgctagc actttgtcac
tgccatcaga ttttccttat agtcttagag tcatgtaaat aaaagttcca taatgaaatt
aaagaaaatt aatttttcta atcttagatc agttccatag aaaactatta atttttttaa
agtaggcagt agaagggggg tgggtggggg tggaattggg tagtaagtct ggttctaata
ttctgagctg cctttggaag gaagttatga ggtagaagat tctactgact tttagtaagg
tggacaatga gagaaaagaa aaagcaggtg cctcatcnnc agatccttnt ggtatttatn
tgccangtnc nanntaatnc atanaaag

```

60
120
180
240
300
360
420
480
540
600
660
688

```

<210> 16
<211> 408
<212> DNA

```

WO 00/37643

PCT/US99/30909

6

<213> Homo sapien

<400> 16

```

cagggtcatca agatgactta caggatgtaa tagggagagc tgtcgagatt ggtgttaaaa      60
agtttatgat tacagggtga aatctacaag acagtaaaga tgcactgcat ttggcacaaa      120
caaatggtat gtttttcagt acagttggat gtcgtcctac aagatgtggt gaatttgaaa      180
agaataaccc tgatctttac ttaaaggagt tgctaaatct tgctgaaaac aataaaggga      240
aagttgtggc aataggagaa tgcggacttg attttgaccc gactgcagtt ttgtcccaaa      300
gatactcaac tcaaataatt tgaaaaacag tttgaaactgt cagaacaaac aaaattacca      360
atgtttcttc attgtccgaa actcacatgc tgaatttttg gacataat      408

```

<210> 17

<211> 407

<212> DNA

<213> Homo sapien

<400> 17

```

ggctcctgggg aggccctagg ggagcaccgt gatggagagg acagagcagg ggctccagca      60
ccttctttct ggactggcgt tcacctccct gtcagtgct tgggctccac gggcaggggt      120
cagagcactc cctaatttat gtgctatata aatatgtcag atgtacatag agatctattt      180
tttctaaaac attcccctyc ccactcctct cccacagagt gctggactgt tccaggccct      240
ccagtgggct gatgctggga cccttaggat ggggctccca gctcctttct cctgtgaatg      300
gaggcagaag acctccaata aagtgccttc tgggcttttt ctaacctttg tcttagctac      360
ctgtgtactg aaatttgggc ctttgatcg aatatggta agaggtt      407

```

<210> 18

<211> 405

<212> DNA

<213> Homo sapien

<400> 18

```

tgaagagtca acttgggcct ggaggactga taaagtttgt gattttgagg gcctctaaaa      60
gtattaaagc agcggcagcc gctgcacgca gacatgagg ctaggttaaa acagtaagat      120
caagttgttt ggacagaaag gctacagagt gtggtcctgg ctcttggtga agaattacga      180
ccacgctaac catgcctagg aaggaaagga gttattgttt tgtagaaagg tgctggggtt      240
tgagagatca gtcggacacg attggcaggg agagcacgtg tgtttttatg agaattatgc      300
ccgagatagg taacagatga ggaagaaatt tgggcttgat tgaagtaatg ggggctgtct      360
tggaagcttt gcagcagtag agcctaggta atttgctgag cctaa      405

```

<210> 19

<211> 401

<212> DNA

<213> Homo sapien

<400> 19

```

tcctgacatt cctgccttct tatattaata agacaaataa aacaaaatag tgttgaagtg      60
ttggggcagc gaaaattttt ggggggtggt atggagagat aatgggcgat gtttctcagg      120
gctgcttcaa gcgggattag gggcggcgtg ggagcctaga gtgggagaga ttaagctgaa      180
gggaggtctt gtggttaagg gtgatatcat ggggatgtta gaagaaacat ttgtcgtata      240
gaatgattgg tgatggcctg gatacggttt tggatgattt gagaagctaa atggaagata      300
caaggtccga ataaaaggag gagaaaaatg ggtattaaat gtctaagaat tgggaggacc      360
taggacatct gattagagag tgcctaagga gattcagcat a      401

```

<210> 20

<211> 331

WO 00/37643

PCT/US99/30909

7

<212> DNA

<213> Homo sapien

<400> 20

```

agggtccagct ctgtctcata cttgactcta aagtcacag cagcaagacg ggcattgtca      60
atctgcagaa cgatgcgggc attgtccaca gtatttgca agatctgagc cctcagggtcc     120
tcgatgatct tgaagtaatg gctccagtct ctgacctggg gtcccttctt ctccaagtgc     180
tcccggattt tgctctccag cctccgggtt cgggtctcca ggctcctcac tctgtccagg     240
taagaggcca ggcggtcgtt caggttttgc atgggtctct tctcgttctg gatgcctccc     300
attcctgcca gacccccggc tatcccggtg g

```

<210> 21

<211> 346

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (346)

<223> n = A,T,C or G

<400> 21

```

gggtccaccac ttgtaccga tatggacttc cggttctct gtccaatgga gccacactaa      60
agatctcacc agtcacgtgg tcaattttaa gccaacctct tgtgtctccc ctcagtgaat     120
agcttatgtc cagaccttct ggatccttgg cagtcacatt gccaccttta gtgcctatag     180
ctacatcctc actgactttc gcttgggaata cgtgttggga aaattgaggt gcttcattca     240
catctgtcac aataagncgt gaacttggca aaagaacttg cattgtactt cacaccaaac     300
actagaggct caggattttc tgctttgaac acaatgttgg aaacag

```

<210> 22

<211> 360

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (360)

<223> n = A,T,C or G

<400> 22

```

gaagactccc tctctcgaa gccggatccc gagccgggca ggatggatca ccaccagccg      60
gggactgggc gctaccaggc gcttcttaat gaagaggata actcagaatc atcggtata      120
gagcagccac ctacttcaaa cccagcacc gcagattgtg caggctgcgt cttcagcacc     180
agcacttgaa actgactctt cccctccacc atatagtagt attactgggt gaagtaccta     240
caacttcaga tacagaagtt tacggtagt tttatccgt gccacctccc tatagcgttg      300
ctacctctct tctacnwtc cgatgaaagc tgagaaggct aaagctgctg caatggcatg      360

```

<210> 23

<211> 251

<212> DNA

<213> Homo sapien

<400> 23

```

ggcggagctc cagcagagc tggaaaagga accttttgag gatggctttg caaatgggga      60
agaaagtact ccaaccagag atgctgtggt cacgtatact gcagaaagta aaggagtcgt     120

```

WO 00/37643

PCT/US99/30909

8

gaagtttggc tggatcaagg gtgtattagt acgttgatg ttaaaccattt ggggtgtgat 180
gcttttcatt agattgtcat ggattgtggg tcaagctgga ataggctctat cagtccttgt 240
aataatgatg g 251

<210> 24
<211> 421
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(421)
<223> = A,T,C or G

<400> 24
caggtctttc ccagggtgtg actccagctc cagcttcagc tccagctcca ggtcgggctc 60
cagctccagc cgcagcttar gcagcgggag gttctgtgtc ccagttgttt tccaatttca 120
ccggtctccg tggatgamcg ygggacctgy caswgctcct gkttycctgc yagsacacca 180
cnytttyccg tggacacrar kggaaackct tggaaattcac agctyatgtt ctttctcara 240
agtttgagaa agaactttct aaagtgaggg aatatgtcca attaattagt gtgtatgaaa 300
agaaactgtt aaacctaact gtccgaattg acatcatgga raaaggatac catttcttac 360
actgaactgg acttcgagct gatcaaggta gaagtgaagg agatggaaaa actggtcata 420
c 421

<210> 25
<211> 381
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(381)
<223> n = A,T,C or G

<400> 25
gaactttttg tttctttatt ttcaatattt gtcttattaa tatttttctt attttataat 60
gcaattacaa caatttagga nacaaaacaa tataaaacaaa agaattgttaa atagtttttt 120
ttaaaaaata gcttggtgct tgcaanaaag tccatataat cttattcccc cccaaatata 180
attttatact ttgcactaaa ccaaaatagc ttatggaaaa ttagtattaa atagctaaac 240
acagaaaacc tacagctata aataacataa aatacagttt aactttaatg ngatgcttaa 300
acaaagcaaa ctatgatgca atattgaatca acttcattaa ttggacaagt ccagnggagg 360
cacaaattag ataagcacta a 381

<210> 26
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 26
ggaaaaggga ctggcctctc tgaagagtga gatgagggaa gtggaaggag agctggaaag 60

WO 00/37643

PCT/US99/30909

9

```

gaaggagctg gagtttgaca cgaatatgga tgcagtacag atgggtgatta cagaagccca 120
gaaggttgat accagaagcc aagaacgctg gggtttacaat ccaagacaca ctcaacacat 180
tagacgggct cctgcattct gatggacca ccttttcang tggtaagatt gaangggg 240
cctgggctta cctgggaagc aaaaactttt cccganccaa ggaaccagg attcaaccan 300
gcnacttgen ggccaaggaa ggcanactn ggaanaaaag gcccttaag caaaagggnc 360
accttcattt gctnggaaan cagcctttan ttggaatctt g 401

```

<210> 27

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 27

```

aattgcaact ggacttttat tgggcagtta cnacaacnaa tgttttcana aaaatatttg 60
gaaaaaatat accacttcat agctaagtct tacagagaan aggatttgct aataaaactt 120
aagttttgaa aattaagatg cnggtanagc ttctgaacta atgcccacag ctccaaggaa 180
nacatgtcct atttagttat tcaaatacca gttgagggca ttgtgattaa gcaaacaata 240
tatttggtan aactttgntt ttaaattact gntncttgac attacttata aaggagnctc 300
taactttcga tttctaaaac tatgtaatac aaaagtatan ntttcccat ttgataaaa 360
gggcnanga tactgantag gaa 383

```

<210> 28

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 28

```

ggtcgcgttt ccctggctc acagtctgcc attatttgca tttttaaatg aagaaaagtt 60
taacgtggat ggatggacag ttacaatcc agtggaagaa tacaggaggc agggcttgcc 120
caatcaccat tggagaataa cttttattaa taagtgtat gagctctgag acacttaccc 180
tgctcttttg gtggttcctc atcgtgcctc anagatgac ctccggagag ttgcaacttt 240
taggtcccga aatcgaatc cagtgtgtgc atggattcat ccagaaaata agacgggtcat 300
tgtgcgttgc agtcagcctc ttgtcggtat gagtgggaaa cgaaataaag atgatgagaa 360
atatctcgat gttatcaggg agactaataa acaaatctct a 401

```

<210> 29

<211> 401

<212> DNA

<213> Homo sapien

<400> 29

```

atatgagttt gccatctcca tggatgcat ttcaatgctt tcagggtaat cattctctcc 60
ccaaagactg cccacggggt catcactcct gtgacgaaat gagggctgga ttgaagatgt 120
tctgctgagc accccctgg tcatctttgg ggtctcagaa gagccataat catgaccatt 180
ctcagcatct gaataatcag gttctctcca agtgcttgcc aagttctgat tgtcctcagc 240

```

actgggatag tctggctccc caaaaaaggg tggagagtta gggtgaatgt cagcgcttg 300
ataatcaggg tttccagag agtctgcgta tggattgatt ctaaaacttg tatgttccag 360
attctttctg gatcctggat gggtcaaatt ggctctgggt c 401

<210> 30

<211> 401

<212> DNA

<213> Homo sapien

<400> 30

cctgaactat ttattaaaaa catgaccact cttggctatt gaagatgctg cctgtatttg 60
agagactgcc atacataata tatgacttcc tagggatctg aaatccataa actaagagaa 120
actgtgtata gcttacctga acaggaatcc ttactgatat ttatagaaca gttgatttcc 180
cccatcccca gtttatggat atgctgcttt aaacttggaa gggggagaca ggaagtttta 240
attgttctga ctaaaacttag gagttgagct aggagtgcgt tcatggtttc ttcactaaca 300
gaggaattat gctttgcact acgtccctcc aagtgaagac agactgtttt agacagactt 360
tttaaaatgg tgccctacca ttgacacatg cagaaattgg t 401

<210> 31

<211> 297

<212> DNA

<213> Homo sapien

<400> 31

acctccatta atgccagggtg ttctctctct gatgccagga atgccaccag ttatgccagg 60
catgccacct ggattgcac atcagagaaa atacaccag tcattttgct gtgaaaacat 120
aatgatgcca atgggtggaa tgatgccacc tggaccagga ataccacctc tgatgcctgg 180
aatgccacca ggtatgcccc cacctgttcc acgtcctgga attcctccaa tgactcaagc 240
acaggctgtt tcagcgccag gtattcttaa tagaccacct gcaccaacag caactgt 297

<210> 32

<211> 401

<212> DNA

<213> Homo sapien

<400> 32

caaacttggg gccaaaaagg acacaaagga ctctcgacce aaactgcccc agacctctc 60
cagaggttgg ggtgaccaac tcactctggac tcagacatat gaagaagctc tatataaatc 120
caagacaagc aacaaacct tgatgattat tcactacttg ggtgagtgc cacacagtca 180
agctttaaag aaagtgtttg ctgaaaataa agaaatccag aaattggcag agcagtttgt 240
cctcctcaat ctggtttatg aaacaactga caaacacctt tctcctgatg gccagtatgt 300
ccccaggatt atgtttgttg acccatctct gacagttaga gcccgatc actggaagat 360
attcaaaccg tctctatgct tacgaacctg cagatacagc t 401

<210> 33

<211> 401

<212> DNA

<213> Homo sapien

<400> 33

agcagagggg caggaatcat tcggccactg ttcagacggg agccacaccc ttctccaatc 60
caagcctggc ccagaagat cacaagagc caaagaaact ggcaggtgtc cagcgctcc 120
aggccagtga gttggttgct acttactttt tctgtgggga agaaattcca taccggagga 180
tgctgaaggc tcagagcttg accctgggcc actttaaaga gcagctcagc aaaaagggaa 240
attataggta ttacttcaaa aaagcaagcg atgagtttgc ctgtggagcg gtgtttgagg 300

WO 00/37643

PCT/US99/30909

11

agatctggga ggatgagacg gtgctcccga tgtatgaagg ccggattctg ggcaaagtgg 360
agcggatcga ttgagccctg gggctctggct ttggtgaact g 401

<210> 34
<211> 401
<212> DNA
<213> Homo sapien

<400> 34
aacaatggct atgaaggcat tgtcgttgca atcgacccca atgtgccaga agatgaaaca 60
ctcattcaac aaataaaagga catggtgacc caggcatctc tgtatctgtt tgaagctaca 120
ggaaagcgat tttatttcaa aaatgttgcc attttgattc ctgaaacatg gaagacaaag 180
gctgactatg tgagaccaa aacttgagacc tacaaaaatg ctgatgttct ggttgcttga 240
gtctactcct ccaggtaatg atgaacccta cactgagcag atggggcaac tgtggagaga 300
aggggtgaaa ggatcccacc tcactcctga tttcattgca ggaaaaaagt tagcttgaat 360
atggaccaca aggtaagggc atttgtccat gaatggggct c 401

<210> 35
<211> 401
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

<400> 35
catttcttcc tactagactg cccccttgat ccactggcag aaatgatggc accaccttgt 60
cttcaggtgg tgctccttca ttattccaag gatgcagcat ctctatggtg ccaggatagg 120
gggtaaagcc tttggcgccc tttccgaat ggcacatcag cagtaaaagt ggtaccaata 180
gcangaacag aaagggcaaa atcatgancc caattgctgc gggccccaa ggcacatagg 240
aatcatgctg ngcttcctg canccgctgc catgcaagac actnacaaac tnggantgta 300
aggacctgct tttcaggaca actaaaaccc tgattgncctg aaatcaggaa ctgaatttca 360
cttctcccaa gctttttctc actttggtgc aacancacac t 401

<210> 36
<211> 401
<212> DNA
<213> Homo sapien

<400> 36
cctgctagaa tcactgccgc tgtgctttcg tggaaatgac agttccttgt tttttttgtt 60
tctgtttttg ttttacatta gtcattggac cacagccatt caggaaactac cccctgcccc 120
acaaagaaat gaacagttgt agggagaccc agcagcacct ttctccaca caccttcatt 180
ttgaagttcg ggtttttgtg ttaagttaat ctgtacattc tgtttgccat tgttacttgt 240
actatacatc tgatatagt gtacggcaaa agagtattaa tccactatct ctagtgttgc 300
actttaaatc agtacagtac ctgtacctgc acggtcaccc gctccgtgtg tcgccctata 360
ttgagggctc aagctttccc ttgttttttg aaaggggttt a 401

<210> 37
<211> 401
<212> DNA
<213> Homo sapien

WO 00/37643

PCT/US99/30909

12

<220>

<221> misc_feature

<222> (1) ... (401)

<223> n = A,T,C or G

<400> 37

cnncntngna atggantnnt tgnctaaaan ganttgatga tgatgaanat ccctangang	60
antaagcatg gancntgatc ntttncnng cactccttta cgacacggaa acangnatca	120
ncatgatggt accaganacc ttatcacna cgcgcacnga nctgactnat tccaaagagt	180
tgnggttacg gncatccggt cattgctcgt gccattgct gcagggtga tinctactggt	240
gcttattatg ntggccctga ggatgctcca caatgaatat aagcatgctg catgatcagc	300
ggcaacanat gctctgccgt ttgcactaca tctttcacgg acacnatntc gaanacgggc	360
acnttgcana gttagacttg gaatgcatgg ngccg .can n	401

<210> 38

<211> 401

<212> DNA

<213> Homo sapien

<400> 38

aattggetca ctctctcaag gcaagcactg tctcaaggca gtctcaaggc agagatgaca	60
cagcaaaaaa cagaggggga gaaaaaagtc tattattggc ttgtgattta caaaagccaa	120
agtccttttag ataaaaggcc aggagtcgta ccaacataga taccaaatcc aggagaacac	180
agaccagcga taagagggac gcttcccat gaccagacc agcctaaagc ccctgtgggg	240
gcagccagtg gggagctgtc agaccttga catggtggtc tttgagaatg ggt.ctgccct	300
tctctccctg accagttggg atagacacct gactggaatc cttgacactg gcagggtgtt	360
ctatgaacag agaggactgt gcctgtcttc ctgaatccca a	401

<210> 39

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (401)

<223> n = A,T,C or G

<400> 39

tctggtangg agcaattcta ttatttgga ttgcatggct gggttgaatt aaaacagggga	60
gtgagaacag gtgagtctag aagtccaaact ctgaaaaggga ccactgtaca ttgaaacaca	120
cggtctgtgt aaagatgctg ctaatgtcag tcaactgggtg cactaaagga tctcttattt	180
tatgtaaaac gttgggaatg acaagatana actgatactc tggttaagtta ccctctgaag	240
ctacttcttg tgaaatacta atgacagcat catcctgcca agcgaaagag gcaggcataa	300
gcaaggacaa attaaaaggg ggtaagagcc ttatcatgat gaggagtctt gttttgacat	360
cttgggaaaa gctgtccata gtgtgaagtc gtcaatttct c	401

<210> 40

<211> 401

<212> DNA

<213> Homo sapien

<400> 40

tctggtcacc caactcttgt ggaagagggg aattgagatc gagtactgaa tatctggcag	60
agaggctgga atccttcagc cccagagccc agggaccact ccagtagatg cagagagggg	120

WO 00/37643

PCT/US99/30909

13

```

cctgcccagg ggtcagggca gtgggtatca ctggtgacat caagaatata agggctgggg      180
aggcattcttt gtttcctggg gccctcctca aagttgctga cactttgggg acgggaaggg      240
gtagaagtag ggctgctcct tttggagctg gagggaaatag acctggagac agagttgagg      300
cagtcgggct gtccaggttc taagcatcac agcttctgca ctgggctctg aggagattct      360
cagccagagg atcccagcct cctcctccct caaatgtcaa g                                401

```

<210> 41

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 41

```

ctggactaaa aatgtccact atggggtgca ctctacagtt tttgaaatgc taggaggcag      60
aaggggcaga gagtaaaaaa catgacctgg tagaaggaag agaggcaaa gaaactaggt      120
ggggaggatc aattagagag gaggcacctg ggatccacct tcttccttan gtcccctcct      180
ccatcagcaa aggagcactt ctctaatacat gccctcccga agactggctg ggagaagggt      240
taaaaacaaa aaatccagga gtaagagcct taggtcagtt tgaaattgga gacaaactgt      300
ctggcaaaagg gtgcganagg gagcttgtgc tcangagtcc agcccgtcca gcctcggggg      360
gtangtttct gaagtgtgcc attggggcct caccttctct g                                401

```

<210> 42

<211> 310

<212> DNA

<213> Homo sapien

<400> 42

```

ggttcgacaa atccccaaaa atggcaaatt aagccctgtg aaaaaataag ttattggatc      60
atacagaaat agcccaaatc tggaaatttt gaattaaaaat tgtaatcctg taaaacaagt      120
tttggggtga atggatttct ttaataccaa taatatTTTT aattcccacc acagatggat      180
ttgctgaata tgctaattgct gtgaatgaga aaacaatttt ggggtaggta taccacaag      240
taatctgatg aaaaaataaa ccacagactg atgtcaaattg gacaaaaaac tgaaaatatg      300
ctgtgagaaa                                310

```

<210> 43

<211> 401

<212> DNA

<213> Homo sapien

<400> 43

```

aggctcactta cacttgtgac cagtgtgggg cagagacctt ccagccgatc cagtctccca      60
ctttcatgcc tctgatcatg tgcccaagcc aggagtgcc aaccaaccgc tcaggagggc      120
ggctgtatct gcagacacgg ggctccagat tcatacaatt ccaggagatg aagatgcaag      180
aacatagtga tcaggtgcct gtgggaaata tcctcgtag tatcacgggt ctggtagaag      240
gagagaacac aaggattgcc cagcctggag accacgtcag cgtcactggt attttcttgc      300
caatcctgcg cactgggttc cgacaggtgg tacagggttt actctcagaa acctacctgg      360
aagcccatcg gattgtgaag atgaacaaga gtgaggatga t                                401

```

<210> 44

<211> 401

<212> DNA

<213> Homo sapien

<400> 44

atccctgtaa	gtctattaaa	tgtaaataat	acatacttta	caacttctct	tagtcggccc	60
ttggcagatt	aaatctttgc	aaaattccat	atgtgctatt	gaaaaatgaa	ataaaacctc	120
agatgtctga	attcttattt	caaatacagt	tatataatta	ttttaaatta	caatatacaa	180
tttctgttaa	atacaactgt	taagggattc	tgagaacaat	tataagatta	taataatata	240
tacaaactaa	cttctgaaat	gacatgggtt	gtttccttcc	cacctccta	ccctctcaaa	300
gagtttttgc	atttgctgtt	cctgggtgca	aaaggcaaaa	gaaaatctaa	aaatagtctg	360
tgtgtgtcca	cgacatgctc	gctcctttga	gaatctcaaa	c		401

<210> 45

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 45

gtgcctgctg	cctggcagcc	tgccctgcc	gctgcctcag	gaggcgggag	gcatgagtga	60
gctacagtgg	gaacaggctc	aggactatct	caagagattt	tatctctatg	actcagaaac	120
aaaaaatgcc	aacagtttag	aagccaaact	caaggagatg	caaaaaattc	tttggcctac	180
ctatactgga	atggtaaact	cccgctcat	anaaataatg	caanaagccc	agatgtggag	240
tgccagatgt	tcagaatac	tactatttcc	caaataagccc	aaaatggact	tccaaagtgg	300
tcacctacag	gatcgtatca	tatactcgag	acttaccgca	tattacagtg	gatcgattag	360
tgtcaaaggc	tttaaacatg	tggggcaaag	agatccccct	g		401

<210> 46

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 46

gtcagaattg	tctttctgaa	aggaagcact	cggaatcctt	ccgaactttc	caagtccatc	60
catgattcan	agatactgcc	ttctctctct	ctgggatttt	atgtgtttct	gatagtgaat	120
tgttgatgta	tttgctactt	tgttcttttt	ctctttcaag	acttgatcat	tttatatgct	180
gnttgagaaa	aaaaagaact	tttggtagca	aggaggtttc	aagaaatgat	tttgattttt	240
ctgctgcgga	atttctcggc	acctacctgt	agtatggggc	acttggtttg	gttgagagt	300
aagaaggtgg	aagaatgagc	tgtacttggt	taagcagttg	aaaccttttt	tgagcaggat	360
ctgtaaaagc	ataattgaat	ttgtttcacc	cccgtggatt	c		401

<210> 47

<211> 401

<212> DNA

<213> Homo sapien

<400> 47

WO 00/37643

PCT/US99/30909

15

```
ggctctgcagc aatgcacttc aaccatacat actgcttcca ctagctaata ccaaatgcag      60
gttctcagat ccagacaaat ggaggaaaag aacatttatg ctcccgtttc agaaagccaa      120
gtcgtagttt tggcccttcc ttctctctaaa gtttattccc aaaaacaggt agcattcctg      180
attgggcaga gaagaggata ttttcagccc acatctgctg caggatgctc atttctctcc      240
atcttactg tgactagtaa agatctcacc acttctcttt ggaatttcca actttgcttg      300
tgattgaatg tcacttcgtg aatttgattt atgtcagatc acttggcatt gctcttccat      360
atgcatcaag ttgccaggca ctaaacccea tgttcatgaa c                          401
```

<210> 48
<211> 430
<212> DNA
<213> Homo sapien

```
<400> 48
acataacttg taaacttttt ctgcttgggg gctgtaacag acagaagagt aaagactaca      60
aggattttct gaagatgctt caatgaaaat catcatttcc tctttagtca tcccaagtct      120
tggtttgaaa aacttgggca tggacttata cagaccttga accaccactg acttatcatt      180
gggtggcaga ccttgaaacc aagctctctg tgttacttct gaaagtgcac caattctgat      240
ttggctaaga acagaagaca aatactggga tcgtgattct gtgttatact ctagccacag      300
catagcagct tctcgaacgg ttcttctcct ttctacattt aaattgtcac tactgagaat      360
atctatcagt aggtcatgtg acagacctgc cccggggccg gcccgctcga tgcttgccga      420
atatcatggt                                     430
```

<210> 49
<211> 57
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (57)
<223> n = A,T,C or G

```
<400> 49
ggtattaaca atatcangca ctcatcttcc cctctttatg aaanggatna attttta      57
```

<210> 50
<211> 327
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (327)
<223> n = A,T,C or G

```
<400> 50
gatggnggtn tccacaagan tnaangtnn tatttaantan nncctttaga nccacttnna      60
ttaattggnn tatgnntgnc ctcttggtgg ntgtngaagc ttcatatnnt ntttggacat      120
cattacacgt cttagctctt tnaagnacaa cttaaagtct atatgaattt tgccattttt      180
gctaacactg gtatgctccn ngcatccacc atnccacntg gaattattta ttncnttcat      240
attaatnttt tgtttaccaa atctnacttg acccgaacga aactttctgn gtattttang      300
gccccnccat tcttactttt caagcct                                     327
```

<210> 51

WO 00/37643

PCT/US99/30909

16

<211> 236
<212> DNA
<213> Homo sapien

<400> 51
cgtctcgaag aagcgctgca ggccgatgat ggactgcacg tctgccttgt cctcagttaa 60
cttgttgaat tgcttgaaca tgcggcccac atcctgggca aactcctgtg gggagctgta 120
gggaggtgac aacttctcct ggaggcgggc acggatcagg gtcagatcca gggtgccacc 180
gggctggtcc agggagaagg tggagtcgta gccagacctg cccgggcggc cgctcg 236

<210> 52
<211> 291
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(291)
<223> n = A,T,C or G

<400> 52
ctcacatcct gggtcgggct gtagagctgc accatggtgc tgagcgcgcc ctccagctcc 60
ttgtagatgt aaaggacggc gaaggagctg tagtctgtgt ccacgatgag cacgtccagg 120
tagcccaagg cggggactct gaagttgtcc ctcgagccc accttcangt actcgggcat 180
ccacctggtt acagccttc gncctcgga actccatntg gactttacag gccgccctcc 240
tctgtgggcc tgatggncct tgcaggacat nggaacacgg gagctcnctt t 291

<210> 53
<211> 95
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(95)
<223> n = A,T,C or G

<400> 53
gtctgtgcag tttctgacac ttgttgttga acatggntaa atacaatggg tatcgctgan 60
cactaagttg tanaanttaa caaatgtgct gnttg 95

<210> 54
<211> 66
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(66)
<223> n = A,T,C or G

<400> 54
cctnaatnat ntnaatggta tcaatnnccc tgaangangg gancggngga agccggnttt 60
gtccgg 66

WO 00/37643

PCT/US99/30909

17

<210> 55
 <211> 265
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (265)
 <223> n = A,T,C or G

<400> 55
 atctttcttc tcagtgccctt ggcctgtgtg agtctatctg gtaacactgg agctgactcc 60
 ctgggaagag aggccaaatg ttacaatgaa cttaa .gat gcaccaagat atatgaccct 120
 gtctgtggga ctgatggaaa tacttatccc aatgaatgcc gtgttatggt tttgaaaatc 180
 ggaaacgcca gacttctatc ctcatcaca aatctgggcc ttcttgaaaa ccaggggttt 240
 naaaatccca ttenggtcnc cggcg 265

<210> 56
 <211> 420
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1) ... (420)
 <223> n = A,T,C or G

<400> 56
 gagcgggcgc cggggcaggt cctcgcggtg acatgatggg atttcaaaac cttgggtctc 60
 agcaaggccc agatttttga atgangatag aagtctggcg ttctcgattt tcaaaacata 120
 acacgcattc atrgggataa gtatttccat cagtcccaca gacngggica tatatcttgg 180
 gtgcattcat taagttcntt tgttaacatt tgggcctctc ttctccangg gaattcagct 240
 cccagttggt taccaanatt naactccacc ggggccaaag gcncttgaaa aaaaaanaa 300
 ttcttgttt accttcctg ggcttnaagt tctggcgctc aaaagttaa tttgaaaact 360
 gcaccgcact taccacgtct cttcnagaan cctggggaca cctcggcgcg gaccacgcta 420

<210> 57
 <211> 170
 <212> DNA
 <213> Homo sapien

<400> 57
 gaagcggagt tgcagcgctt ggtggccgcc gagcagcaga aggcgcagtt tactgcacag 60
 gtgcattcat tcatggagt atgttgggat aaatgtgtgg agaagccagg gaatcgcccta 120
 gactctcgca ctgaaaattg tctctccaga cctcggcgcg gaccacgcta 170

<210> 58
 <211> 193
 <212> DNA
 <213> Homo sapien

<400> 58
 attttcagtg cgagagtcta ggcgattccc tggcttctcc acacatttat cccaacataa 60
 ctccatgaag tgatgcacct gtgcagtaaa ctgcgccttc tgctgctcgg cggccaccag 120
 gcgctgcaac tccgcttcat cggcttcgcc cagctccgcc attgttcgcc acctgcccgg 180

WO 00/37643

PCT/US99/30909

18

gcggccgctc gaa 193

<210> 59
<211> 229
<212> DNA
<213> Homo sapien

<400> 59
cgcaactctc gagcatttat atacaatagc aaatcatcca gtgtgttgta cagtctataa 60
tactccaaca gtctcccatc tgtattcaat ggcgccaccc aatacagtc tttgtttgga 120
tgctggggag agtaatccct accccaagca ccatatagat aagaaaaccc tctccagttg 180
agctgaacca cagacggttt gctgatacct gcccgggcgg ccgctcgaa 229

<210> 60
<211> 340
<212> DNA
<213> Homo sapien

<400> 60
tcgagcggcc gcccgggcag gtccctctaaa gatcaaaaca cccctgtcgt ccacctcct 60
cccactccag ggaagctgtg gtcattggtg gtgtgtgaac atcagcaaac cgtctgtggt 120
tcagtcgaac tggagagggt tttcttatct atatggtgct tggggtaggg attactctcc 180
ccagcatcca aacaaaggac tgtattgggt ggcgccattg aatacagatg ggaaactgtt 240
ggagtattat aaactggtac aacacactgg atgatttgct attgtatata aatgctcgag 300
aattgcggat cacctatgga cctcggccgc gaccacgctg 340

<210> 61
<211> 179
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(179)
<223> n = A,T,C or G

<400> 61
tttttgtgac ggacgnttg agtacatgtc ccaggatcac atccagcagc tagagtggct 60
gggacaagct ggcgngggcc aagcactgtt gaaacnatag gggctctgggn gnactcgggt 120
tnaagtgggt ggtccgantn ttnataacct tgtcngaacc nancatctcg gttgncang 179

<210> 62
<211> 78
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(78)
<223> n = A,T,C or G

<400> 62
agggcgttcg taacgggaat gccgaagcgt gggaaaaagg gagcgggtggc nggaagacgg 60
ggatgagctt angacaga 78

WO 00/37643

PCT/US99/30909

19

<210> 63
<211> 410
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(410)
<223> n = A,T,C or G

<400> 63
cccagttact tggggaggct gaggcagggg gaatcctttg aacccggngg gtgggaggtt 60
gcagtgagcc cgagatagca ccattgcact tccancatgg ggtggacaga gtgagactct 120
atctcaaaaa aaaagaaaag aaaaggaaaag agattagatt aagattaagt acctacttcc 180
tntcccatTT caagtcttga aaatagagga tcagaaatgt tgaggaattc tttaggatag 240
aaagggagat gggattttac ttatggggaa agaccgcaaa taaagactgn aacttaacca 300
cattccccaa gtgnaagggtg ttacccaaga agtaggaacc cttttggctn ttaccttacc 360
ttccngaaaa aaacttattn cttaaaatgg aaacccttaa agcccgggca 410

<210> 64
<211> 199
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(199)
<223> n = A,T,C or G

<400> 64
cttgttctca aaaagggtcaa agggagccccg acgaggaata aatagcaatg ccctgaattc 60
caactgacct tctacagaaa agtgcttgac tgccaagtgg tcttcccagt cattagttag 120
gctcttgtag aattctccat actcctcttg ggngangnca tnagggttn nggccccaaat 180
aggntgggcc tngttaagt 199

<210> 65
<211> 125
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(125)
<223> n = A,T,C or G

<400> 65
agcggtagag ttctgtcctg gcatcatcat tcattgtagt atgggtcaata ggtgccatga 60
aactcagtag cttgctaagg acatgaaacc gaagtttctt gcctttgctg gcctngtngn 120
gggta 125

<210> 66
<211> 204
<212> DNA
<213> Homo sapien

WO 00/37643

PCT/US99/30909

20

```

<400> 66
attcagaatt ctggcatcgg tattttctata aagtccatca gttagagcag gagcaggccc      60
ggaggggacgc cctgaagcag cgggcggaac agagcatctc tgaagagccc ggctgggagg      120
aggaggaaga ggagctcatg ggcatttcac ccatatctcc aaaagaggca aaggttcctg      180
tggacctcgg ccgcgaccac gcta                                           204

```

```

<210> 67
<211> 383
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

```

```

<400> 67
tcagggcctc caggcagcca gttttgcagg anattcagca cctagngtct tcctgcctna      60
cgctcccaag aacctgctcc tgcaggggga acatcagaac tcgtccttga tgtraaaatg      120
gggctggctc tnaggcttga agtccagggt agggctgcca tcctcattga gaattctccg      180
ggcagtgtan ccgacgatgg ggtatttggc ttgtacact ttggtgaaaa cctnatccag      240
ggcctccagt tccttggccg tganaccggt antgtcatgg gtgaggtctg caggatccaa      300
ggacatcttg gctaccctc tagtggagtc cttccccgtc aaggcattgt aaggggctcc      360
tcgtccataa aactcctttt cgg                                           383

```

```

<210> 68
<211> 99
<212> DNA
<213> Homo sapien

```

```

<400> 68
tcacatctcc tttttttttt aactttttca aatttttgtg ttaaatagaa ggctaaaggg      60
ttagatttaa gtttctgcta cattgaccct atttaccta                               99

```

```

<210> 69
<211> 37
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(37)
<223> n = A,T,C or G

```

```

<400> 69
gagaaggacn tacggncctg ntantanang aatctcc                                37

```

```

<210> 70
<211> 222
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(222)

```

WO 00/37643

PCT/US99/30909

21

<223> n = A,T,C or G

<400> 70

```
gtgggtcatt tttgctgtca ccagcaacgt tgccacgacg aacatccttg acagacacat      60
tcttgacatt gaagcccaca ttgtccccag gaagagcttc actcaaagct tcatggcgca      120
tttcgacaga ttttacttcc gttgtaacgt tgactggagc aaaggtgacc accataccgg      180
gtttgagaac acccantcac ctgccccggg cggccgctcg aa                          222
```

<210> 71

<211> 428

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(428)

<223> n = A,T,C or G

<400> 71

```
caggagtatt ttgtagaaaa gccagaagag cattagtaga tgtatggaaa tatacggtag      60
ggcacacgct gacagtactt ttccaagcc acgccgtatt tcttcttaca gtggtactcg      120
tcacgagctt ctcggtggac aagcaacatg gtgaaataaa ttatgtagaa ataaggcaga      180
atgtggttaa aaccacatgg gagggaccac gccaaaggcca tgatgagatc acccaagtaa      240
ttgggggtggc gaacaaagcc ccaccatcca gaaactagaa naatttttcc cgttgaaata      300
tgaatggntt ttaaattgtc aagctttgga tcaactgggaa ttttcccgaa tgcctttttc      360
tganaattgc accttnggaa gantccttac cccaagnttc agaccattat ttnaaaagcn      420
ttggaact                                          428
```

<210> 72

<211> 264

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(264)

<223> n = A,T,C or G

<400> 72

```
gaataaagag cttactggaa tccagcaggg ttttctgccc aaggatttgc aagctgaagc      60
tctctgcaaa cttgatagga gagtaaaaag ccacaataga gcagtttatg aagatcttgg      120
aggagattga cacactgat cctgccagaa aatttcaaag acagtagatt gaaaaggaaa      180
ggcttttggt aaaaaagggt caggcattcc tagccgantg tgacacagtg gagcanaaca      240
tctgcangag actgancggc tgca                          264
```

<210> 73

<211> 442

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(442)

<223> n = A,T,C or G

WO 00/37643

PCT/US99/30909

22

<400> 73

ggcgaatccg	gcgggtatca	gagccatcag	aaccgccacc	atgacggtgg	gcaagagcag	60
caagatgctg	cagcatattg	attacaggat	gaggtgcatc	ctgcaggacg	gccggatctt	120
cattggcacc	ttcaaggctt	ttgacaagca	catgaatttg	atcctctgtg	actgtgatga	180
gttcagaaag	atcaagccaa	agaacttcaa	acaagcagaa	aggggaagaga	agcgagtcct	240
cggctctgng	ctgctgccaa	gggagaatct	ggtctcaatg	acngtagaag	gaccttcttc	300
caaagatact	ggnattgctc	gagttccact	tgctggaact	tcccggggcc	caaggatcgc	360
aaggcttctg	gcaaaagaaa	tccanacttn	ggccgggacc	acctaanca	attcacacac	420
tggcgccgt	actagtggat	cc				442

<210> 74

<211> 337

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(337)

<223> n = A,T,C or G

<400> 74

ggtagcagcg	tctccagagc	ctgatctggg	gtcccagata	cccaggcagc	agcagccctg	60
gaggtaaag	gcaagctccc	caatgtgagg	ggagacccca	ttcctggtca	gccaggcttt	120
cagaggagat	agcaggtcga	gggagccaac	gaagaagaga	ctgccancag	gggaaggact	180
gtcccgcmaa	ggacagaact	gattcagggg	ggtcaatgct	cctctagaga	agagccacac	240
agaactgggg	gggccaggaa	ccatgaanct	tggctgtggt	ctaaggagcc	aggaatctgg	300
acagtgttct	gggtcatacc	aggattcttg	aattgta			337

<210> 75

<211> 588

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(588)

<223> n = A,T,C or G

<400> 75

catgatgagt	tctgagctac	ggaggaaccc	tcatctcctc	aaaagtaatt	tatcttttaca	60
gcttctggtt	tcacatgaaa	ttgtttgcgc	tactgagact	gttactacaa	acttttttaag	120
acatgaaaag	gcgtaatgaa	aaccatcccc	tccccattcc	tctcctctc	tgagggactg	180
gaggggaagc	gtgcttctga	ggaacaactc	taattagtag	acttgtgttt	gtagatttac	240
actttgtatt	atgtattaac	atggcgtggt	tatcttttga	tttttctctg	gttgggagta	300
tgatatgaag	gatcaagatc	ctcaactcac	acatgtagac	aaacattagc	tctttactct	360
ttctcaaccc	cttttatgat	tttaataatt	ctcacttaac	taatttttga	agcctgagat	420
caataagaaa	tgttcaggag	agangaaaga	aaaaaaatat	atgttcccca	tttatattta	480
gagagagacc	cttantcttg	cctgcaaaaa	gtccaccttt	catagtagta	ngggccacat	540
attacattca	gttgctatag	gncagcactg	aactgcatta	cctgggca		588

<210> 76

<211> 196

<212> DNA

<213> Homo sapien

WO 00/37643

PCT/US99/30909

23

```

<400> 76
gcggtatcac agcctggccc ccatgtacta tcggggggcc caggctgcc tctgtgtcta    60
tgacatcacc aacacagata catttgcacg ggccaagaac tgggtgaagg agctacagag    120
gcaggccagc cccaacatcg tcattgcact cgcgggtaac aaggcagacc tggacctgcc    180
cgggcggccg ctcgaa                                         196

```

<210> 77

<211> 458

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(458)

<223> n = A,T,C or G

```

<400> 77
agtagagatg gggtttcact gtgttaacca ggatggctct gatctcctgg cctcgtgac    60
tgcccgccct ggctcccaa agtggtggga ttacaggcgt gaaccaccgc acccggccag    120
aaatgttagt ttttcctat tctctcctt ttttcctatt atatacttg tcaaccagac    180
agccatccta cccanaatg gtaatgcctc ttcattcctc atatgaggga ataaaagaga    240
aaaaagcttt tggaaaacat ccacttatct aatcatccca aatatgtaat caaaagtata    300
caactcatgt gaagaatata ctggtaaaat gttantatag gccaaaggtat cttgaattcc    360
tatatagaaa gctggtaaat gcccttttgg ctggaaccgc catcttcnn taattcnccc    420
aaaatgacca aacacaaagg gnaagangan aagccccc                                         458

```

<210> 78

<211> 464

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(464)

<223> n = A,T,C or G

```

<400> 78
tccgcaaatt tctgcccgc aagggtccag catttgaggg tgatgatgga ttctgtgtgt    60
ttgagagcaa cgccattgcc tactatgtga gcaatgagga gctgcgggga agtactccag    120
aggcagcagc ccagggtggg cagtgggtga gctttgctga ttccgatata gtgccccag    180
ccagtacctg ggtgtcccc accttgggca tcatgcacca caacaaacag gccactgaga    240
atgcaaagga ggaagtgagg cgaattctgg ggctgctgga tgcttacttg aagacgagga    300
cttttctggt gggcgaacga gtgacattgg ctgacatcac agttgtctgc accctgttgt    360
ggctctataa gcaggntcta gaaccttctt ttgcangac cttcggccgg accacgctta    420
acccaaattc cacacacttg cnggccgtac taanggaatc ccac                                         464

```

<210> 79

<211> 380

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(380)

<223> n = A,T,C or G

24

cgacc	agttttttcca	tctccttcac	ttctaccttg	atcagctcga	agtcacagttc	60
aagaa	atgggtatcct	tctccatgat	gtcaattcgg	acagtttaggt	ttaacagttt	120
catac	acactaatta	attggacata	ttccctcact	ttanaaagtt	cttttctcaa	180
ganaa	aagaacatga	actgtgaatt	ccaagcggtc	ccactctgtc	cacgggaaaa	240
tgctc	ggcagggaaa	cagaacactg	gcagggtccac	ggtcatccac	ggagccgggtg	300
gggaa	aacaactggg	acacagaacc	tccgctgcct	aagctgcggn	tgggagcttg	360
cgacc	tggaactgga					380

<213> Homo sapien

<223> n = A, T, C or G

tcgagcgggc	gcccgggcag	gtcttcagag	agctgtttgt	tncgtttctt	caaaaactcc	60
tattctccac	ttctgctaaa	ggactggatg	acatcaattg	tgatagcaat	atttgtgggt	120
gttctgtcan	ncancatcgc	actcctgaac	aaagtagatg	ttggattgga	tcagttctct	180
tccaccgga	tgactctcan	atgggtggatn	atttcaaact	catcantcag	tacctgcctg	240
cngggtccgc	gtctgttctt	atgtctgcag	gangggcnct	actacacttc	ttcnagggg	300
canaacatgg	tgtgcngcgg	ccatgggtcg	gcaacantga	ttcnctgctg	caccanatn	360

<213> Homo sapien

<223> n = A, T, C or G

acgtgggtccg	gcgagttctga	cctgcagata	tgaactcctt	gggaaacctt	cattctgcct	60
cagacatact	gggggcaaatt	ggcttttaaaa	gtctgggtca	gggagccaag	attacagaaa	120
nccgttgagt	cncatacat	ggacactgac	aaaggaaactg	aagatatcca	aacaagccct	180
cctgggtccc	ngcctgcata	aagatcggga	ncggaacggt	accngacgtc	tgtggtcagg	240
ggttggtggaa	aattggaaaa	aaccagtcct	gcccacattg	acagggaagc	ctcaacggaa	300
attgaacaga	tngtcttatc	accagtcctc	cctcctggat	cntgtctcgg	ctcnggggan	360
tcagtgtaca	gtcctttcag	gtggaagaag	caaagaagat	caacaanaag	cngatcctct	420
cacctgntac	cagcatatgg					440

<213> Homo sapien

<221> misc feature

PCT/US99/30909

<223> n = A, T, C or G

agcgtgggtcg	cggccgangt	cctgacattc	ctgccttctt	atattaatta	tacnaataaaa	60
acaaaatagt	gttgaagtgt	tggagcggcg	aaaatttttg	gggggtggta	tggacagaga	120
atgggcgatn	tctctcanggc	tgcttcaagt	gggattgggg	cngcgtggga	tcatncagtg	180
gganagattn	ccttgaccgg	antctnttgg	tanggatnat	cttgtgggga	tgtgcaagag	240
ncattcgtct	cctgaatgan	tggt				264

<213> Homo sapien

<223> n = A, T, C or G

ancgtgggtcg	cggccgangt	ccacagttgt	gggagagcca	gccattgtgg	gggcagctcc	60
acaggtaaga	ctcgtgtcct	gagcagcgca	catcatccag	gacaaatgggt	cctgagccct	120
gaccaaaccg	ggcatttcct	ggggctgaca	tggcccgacc	acagcccant	tgcttgacaga	180
cgaaatggc	atcattgggt	tcccagtant	catcacacac	ggtgccccag	gaacctccgg	240
tatangaact	ccactcgcc	ctnanacctg	tgccctccat	tcncagcct	cagggggcaa	300
actgggattc	agatccttct	gtgggtacag	gtggtgatat	cctgacaggc	caactttctg	360
gcctgagtgt	tgactgangc	tgggcagacc	tgcccgggcg	gccgctcgaa		410

<213> Homo sapien

<223> n = A, T, C or G

tccaacggcc	gcccgggag	gtctgcccc	ggtgatcca	tttgccgcg	atctctatca	60
naaggagctg	gctaccctgc	nncgacgaan	tcctgaanat	aatctcacc	nccagatct	120
ctctgtcgca	atggagatgt	cgtcatcggt	ggncctgatc	acagggcatt	ggactcagag	180
anangtnanc	acagtgtna	agcgattgan	nnagttcagt	tgctgggtctt	acccgatntt	240
ggaaggaagg	aaaacgtgt	angacgtatc	tcgatgnant	tgaccaaanc	tgaangctnc	300
agggggcatc	gcaaaganan					320

<213> Homo sapien

$\langle 222 \rangle$ (1) ... (218)

WO 00/37643

PCT/US99/30909

26

<223> n = A,T,C or G

<400> 85

```
tcgagcggcc gcccgggcag gtctgctgcc cgtgctggtg ccattgcccc atgtgaagtc      60
actgtgccag cccagaacac tggctctcggg cccgagaaga ctcccttctc caggctntan    120
gtatcaccac taaaatctcc aggggcacca tnganactct gggtgtccgc aatgttgcca      180
atgtctgtcc gcnattggc tacccaactg ttgcatca      218
```

<210> 86

<211> 283

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(283)

<223> n = A,T,C or G

<400> 86

```
tcgacttctt gtgaaggttt tgganaaata tgtatcagtt cgttttattt gggatttcaa      60
taatattctt ggtgataatg ctgactccat ggcttctgac cccaaaaatt gacctgtctg    120
ccactggttg tagccttgag attgattttt gtagccaaga ttgtttcttc gtcctctgaa      180
gtactggttg tanttcctc tgnngggcat tccctctctg tgtantccc tctgtttgan      240
taactaccac ggccaggaaa aacaggggca cgaaggtatg gat      283
```

<210> 87

<211> 179

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(179)

<223> n = A,T,C or G

<400> 87

```
agcgtggtcc cggccgatgt ctttctgtgt aagtgcataa cactccacat acttgacatc      60
cttcangtca cgggccagct nttcagcant ctctggagtg ataggctact gtntgttcln    120
ggcaagtgtc tcaanaatac aggggtcntc tctgagatga ntttcagtcc cgaaccctc      179
```

<210> 88

<211> 512

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(512)

<223> n = A,T,C or G

<400> 88

```
tcgagcggcc gcccgggcag gtcctanacan agaataccca aatttatgga gagttaacag      60
gggtttaaca ggaangaagt gccttttagta agttctcaag ccagangctg gaggcagcag    120
ctaaatcaga ggacaggatc ctcaagtgaat gtgagccatt cggggtggca tgtcactcca      180
ggaataagca caacttanaa acaaatgatt tcgtangata gcacagtgc attggtgcac      240
```

WO 00/37643

PCT/US99/30909

27

```

ttgtgaacct gaggccactg tgtcaaaactg tgcactgggt gtgaataggg aganccaaaa      300
attatgtcct actgggtaat gagcttttcaa tgggctcgat cctctcacnc tgaaagctct      360
gtagagcagc tcagaaccac aaccactccc aacattgacc cttctggggg tactgtctgt      420
ggcaccacaca ggaaggagct ggagatcccc attaggactg tccaccacaca cttgaagcca      480
caaaactgca cctcggccgc gaccaccgct ta                                     512

```

```

<210> 89
<211> 358
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(358)
<223> n = A,T,C or G

```

```

<400> 89
tcgagcgggc cgccccggca ggtctgccag tccccatccc agacattctt tgcattctaag      60
ctgangtctg aactgagtgg ggtgggctgg tgtttccatc ctcacaactc cagtgagccg      120
ggtgtggcgg tggcctgcgt ctctctggcg gttagtgatg ttggcatcat ccaccttttt      180
caaaacaaaa gcactggact gaagaanaat cccnccctgt ntccaccacg tccatggttt      240
ttaataaaaag ggttatnnaa gttgancaag ncatcaccac acacaancct aagaacnttt      300
ttcatcnntc cccaaaacaa acccncaccc tgggaactcc gggcgcgaac cagcgcta       358

```

```

<210> 90
<211> 250
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(250)
<223> n = A,T,C or G

```

```

<400> 90
cgagcggcgg cccgggcagg tctggatggg gagacggact ggaactgcgg cttcccgtgg      60
cctgcacgca caaggctccc caggccggcc gaccttcttc agattcgatc gtatgtgtac      120
gcacnaagag ccaaattattg acattcaca cttcgtggga atnttaccac anaagactgc      180
gaccccccca tcaggcgana gcctgagcat agaagaacac cgctgtgggc ttggcactgt      240
gggncccatc                                     250

```

```

<210> 91
<211> 133
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(133)
<223> n = A,T,C or G

```

```

<400> 91
tcgagcggcc gnccgggcag gtcccgggtg gttgtttgcc gaaatgggca agttcntnaa      60
nctggggaag gtgggtcntg tncgtgctgg acgctactcc ggacgcnaag ctgtcntcgt      120
gangancatt gat                                     133

```

WO 00/37643

PCT/US99/30909

28

<210> 92
<211> 232
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (232)
<223> n = A,T,C or G

<400> 92
agcgtgggtcg cggccgangt ctgtcacttt gcgggggtag cgggtcaattc cagccaccag 60
agcatggctg taggggcat ctgaggtgcc atcatcaatg ttcttcacga tgacaagctt 120
tgcgtccgga gtagcgtcca gccaggacaa gcaccacctt cccacgtntt cangaactng 180
cccatctcgg cataaccacc cgggacctgc ccgggcggnc gctcgaaaag cc 232

<210> 93
<211> 480
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (480)
<223> n = A,T,C or G

<400> 93
agcgtgggtc gcgccgang tctgtangct caccggccag agaagaccac tgtgagcatt 60
ttgccgtata tctgtccctg ccatttgctt acttttttaa ctaaaatagg aacatccgac 120
acacaccgtt tgcctcgtct tctcccttga tattttaagc attttcccat gtcgtgagtt 180
tctcagaaac atgtttttta caattgtact atttagtcat ngtccattta ctataattta 240
tctgaccatt tccctactgt taaaatactt aagacgggtt ctgatttttc cactatntaa 300
ataatgctgt gatgaatct tttaaaatct tctgatttct tacttttttc ccccttagat 360
gcctggaagt ggtattttga ggtgaaagag tttgttcatt ttgaanatat ttctgtctct 420
ctctcgacct gatgtgtana cgctcacttc cagttagcag aaccacctta gtttgtgtct 480

<210> 94
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (472)
<223> n = A,T,C or G

<400> 94
tcgagcggnc gccggggcag ggtctgatgt cantcacaac ttgaagggat gccaatgatg 60
taccaatccn atgtgaaatc tctcctctta tctcctatgc tgganaaggg attacaaagt 120
tatgtggcng ataannaatt ccatgcacct ctantcatcg atgagaatgg agttcatgan 180
ctggtgaacn atggtatctg aaccgatac cangttttgt ttgccacgat angantagct 240
tttatttttg atagaccaac tgtgaacctt ccacacgtct tggacnactg anntctaact 300
atccncaggg ttttattttg cttgttgaac tcttncagct nttgcaaact tcccaagatc 360
canatgactg antttcagat agcattttta tgattccan ctcattgaag gtcttatnta 420

WO 00/37643

PCT/US99/30909

29

tntcntttttt tccaagccaa ggagaccatt ggacctcggc cgcgaccacc tn 472

<210> 95

<211> 309

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(309)

<223> n = A,T,C or G

<400> 95

tgcagcggcc gcccgggcag agtgtcgagc cagcgtcgcc gcgatgggtgt tgttgagag	60
cgagcagttc ctgacggaac tgaccagact tttccanaag tgccggacgt cgggcancgt	120
ctatatcacc ttgaagaant atgacggtcg aaccaaacc attccaaaga aangtactgt	180
gganggcttt gancccgag acaacnagtg tctgttaaga actaccgatn ggaaanaana	240
anacagcac tgtgggtgag ctccnaggga agttaataan tttcggatgg gcttattcna	300
acctcctta	309

<210> 96

<211> 371

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(371)

<223> n = A,T,C or G

<400> 96

tgcagcggcc gcccgggcag gtccaccact cacctactcc ccgtctctat agatttgctt	60
gttctgggca gttctcagca atggaatcct actgtgtatc tttttgtgac tggttcttta	120
actcagcatc acattttcaa ggttcaccca tgctgcagcc tggctccgta ctggtgacag	180
tacttcattt ctctctccct tttgttcaga ccaaggtctc cctctgtccc caaggctaaa	240
gtgcagttgg tgtgatcatg gctcactgca gcctcaaact cctggactca aacagtcctc	300
ccatctcagc ctcccaaagt gctgatntta taagttgcaa gcctgcacc cagcctgtat	360
ctccagtttg t	371

<210> 97

<211> 430

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(430)

<223> n = A,T,C or G

<400> 97

tgcancggcc gcccgggcag gttnttttn tttnttttt nnnngntagt atttaagan	60
atttattaaa tcatcttat accaaaatgg aaacatnttc caactagaaa catgcnacca	120
tcatcttccc cagtcagtc ncaangtcca atattttntc tgctctgca gataaaaagt	180
tcnnattttt ataccactc ttactcccc caaaaatntt aattcngtcc tncctaaaa	240
ttncnccggg taacaantta caaaaatggc naaccaatta ttttaanaa aagttgcncn	300

WO 00/37643

PCT/US99/30909

30

```

ttnaaaangg aaactttntg gcaanttanc ctcttttccc ttcccacccc ccantttaag      360
gggaaaacaa tggcactttg ctcttgcttn aacccaaaat tgtcttccaa aaactattaa      420
aatgttnaa                                     430

```

```

<210> 98
<211> 307
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(307)
<223> n = A,T,C or G

```

```

<400> 98
tcnaacggcc gcccnngcnn gtctngcngc acctgtgcct canccgtcga tacctggtcg      60
attgggacan ggaanacaat ntggttttca gggaggccac anatttggag aaacggatga      120
attctccttt attccgaant cagctccttg gtctccgtag anggtgatct tgaaattctc      180
ctgttttgaa aactttcttg aanaaacctt acctgctggg tgtatttggg ctcccactcg      240
gacaagtact cgttatccnn ggtactctta atgtgcccac gtnaactccc cgggntggca      300
actggaa                                     307

```

```

<210> 99
<211> 207
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(207)
<223> n = A,T,C or G

```

```

<400> 99
gtccnggacc gatgttgchn aganntttct tgggtccanta gggtcnaaaa aatgataanc      60
naggntnanc acgtgaagat ntntatanag tcttantnaa aacnctaga tctgnatgac      120
gataantcga anacnggggg aggggntgag gngaggtggn gtganggaag anntgttgat      180
aaaaganna gntgataaga annagc                                     207

```

```

<210> 100
<211> 200
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(200)
<223> n = A,T,C or G

```

```

<400> 100
acntnnacta gaantaacag ncnttctang aacactacca tctgtnttca catgaaatgc      60
cacacacata naaactccaa catcaatttc attgcacaga ctgactgtaa ttaattttgt      120
cacaggaatc tatggactga atctaatgcn nccccaaatg ttgttngttt gcaatntcaa      180
acatnnttat tccancagat                                     200

```

```

<210> 101

```


WO 00/37643

PCT/US99/30909

31

<211> 51
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(51)
 <223> n = A,T,C or G

<400> 101
 tcgagcgggcc gcccgggcag gtctgaccag tgganaaatg cccagttatt g 51

<210> 102
 <211> 385
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(385)
 <223> n = A,T,C or G

<400> 102
 aacgtgggtcg cgcccgaaagt ccatgggtgct gggattaatc cactgtgacn gtgactctga 60
 gttgagttgt ttttcaatct tctccaagcc tgtggactca tcctccacat ccttgggtag 120
 taggatgaac atgctgaaga tgctnatttt gaaaagggaac tctatgaatc ttacaattga 180
 atactgtcaa tgtttcccca tnacagaacg tggnccecca aggttccatc atctgcactg 240
 ggtttgggtg ttctgtcttg gttgactctt gaaaagggaac atttcttttt gttttcttga 300
 attcanggae attttcttca tccactttgc ccacaaaagt taggcagcat ttaaccccca 360
 anggattttg ggtctgggtc cttec 385

<210> 103
 <211> 189
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(189)
 <223> n = A,T,C or G

<400> 103
 agcgtgggtcg cgcccgaaagt ctgcagcctg ggactgaccg ggaagctctg attatttacc 60
 caccacaggt angttgtgtt ctgaatctca agttcacagg ttaaggctac agcatcctca 120
 tcctccacgg ggttggantt gttgctggtg atgaanggtt tggggtggct ctgcataact 180
 gttgatctc 189

<210> 104
 <211> 181
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(181)
 <223> n = A,T,C or G

WO 00/37643

PCT/US99/30909

32

<400> 104

tcgagcggcc gcccgggcag gtccaggtct ccaccaangc accaccgtgg gaagctggta	60
attgatgccc accttgaagc cnntggggca ccaccncca actggatgct gcgcttggtt	120
ttgatgggtg caatggcaca ttgactcttt tgggaaccac ttcaccacgg tacaacaggc	180
a	181

<210> 105

<211> 327

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(327)

<223> n = A,T,C or G

<400> 105

tcgagcggcc gcccgggcag gtcttctgtg gagtctgcgt gggcatcgtg ggagtgggg	60
ctgccctggc cgatgctcan aaccccagcc tctttgtaa gattctcatc gtgganatct	120
ttggcagcgc cattggcctc tttgggggtca tcgtcgcaat tcttcanacc tccanaatga	180
anatgggtga ctanataata tgtgtgggtg gggccgtgcc tcacttttat ttattgctgg	240
ttttcctggg acagaactcg ggcgcgaaca cgcttanceg aattccaaca cactggcggg	300
cgttactagt ggatccgagc tcggtac	327

<210> 106

<211> 268

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(268)

<223> n = A,T,C or G

<400> 106

agcgtggctg cggccgangt ctggcgtgtg ccacatcggt cccacctcgc tttacaaaac	60
agtcctgaac ttnatctaataaaaattattg tacacnacat ttacattaga aaaaganagc	120
tgggtgtang aaaccggggc tgggtgtccc ttttaagcgaa ngtggctcca cagttggggc	180
atcgctcgtt cctcnaagca aaaacgcaa tgaacccna aggggggaaaa aggaatgaag	240
gaactgnccn gggargnccg ctccgaaa	268

<210> 107

<211> 353

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(353)

<223> n = A,T,C or G

<400> 107

tcgagcggcc gcccgggcag gtggccaggc catgttatgg gatctcaacg aaggcaaaca	60
cctttacacn ctagatgggtg gggacatcat caacgcctg tgcttcagcc ctaaccgcta	120

WO 00/37643

PCT/US99/30909

33

```

ctggctgtgt gctgccgcag gccccagcat caagatctgg gatttanagg gaaagatcnt 180
tgttnatgaa ctgaancnta aattatcagt tccannacca ngcaaaaacc acccngtgca 240
ctccctggcc tggctctgctg atgggacctc gggcgcgaaac acgctnancc caattccanc 300
acactgggcg gncgttacta ntggatccga actcnggtac caancttggc gtt 353

```

<210> 108

<211> 360

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(360)

<223> n = A,T,C or G

<400> 108

```

agcgtggtcg cggccgaagt cctggcctca catgaccctg ctccagcaac ttgaacagga 60
naagcagcag ctacatcctt aaggtccgga aagtttagatg aagatttggga tcctgcattg 120
ncctgcctcc cacctatctc tcccnatta taaacagcct ccttgggaag cagcagaatt 180
taaaaactct cccnctgccc tnttgaacta cacaccnacc gggaaaacct ttttcanaat 240
ggcacaaaaa tcnagaggaa tgcatttcca tgaangaana aactgggtta cccaaaatta 300
ttgggttggg gaaatccngg gggggttttn aaaaaagggc aancnccaa anaaaaaac 360

```

<210> 109

<211> 101

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(101)

<223> n = A,T,C or G

<400> 109

```

atcgtggtcn cggccgaagt cctgtgtcct ggatgggccc tgtgcancga atccgttggc 60
gactcctaac taccaanaaa angactctcg gaagaaattt c 101

```

<210> 110

<211> 300

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(300)

<223> n = A,T,C or G

<400> 110

```

ccanggaaac ccagagtcac atgagatagg gtggctttcg ggacaggggg tcagangaat 60
ggtacatgga tctcagcccc tgatggacac ggaacagggtg tggtcagaac tcccangatt 120
ctgcatccan gatccagtct ctatagaagt tatggatcat tccttcattt cattcccccc 180
ttcatgaaaa aacttctgaa caagcctttt ttctcacttt ggggccctgt ttggcncaag 240
gtnttnantt ggggaaaaaa aaacaaatcc ntccnttan ccctccgtgg ggaatgacct 300

```

<210> 111

PCT/US99/30909

```
<211> 366
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(366)
<223> n = A,T,C or G
```

```
<210> 112
<211> 405
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(405)
<223> n = A,T,C or G
```

```
<210> 113
<211> 401
<212> DNA
<213> Homo sapien
```

```
<210> 114
<211> 401
<212> DNA
<213> Homo sapien
```

WO 00/37643

PCT/US99/30909

35

```

<220>
<221> misc_feature
<222> (1)...(401)
<223> n = A,T,C or G

```

```

<400> 114
angtccacag gangcangag gccaggctcc gtcccancca gtccatgatg ttgaagagga      60
ggaagcagca catgggggtg aagaactgac tccacttccc aggactggtg gagctggtca     120
ccatggctgt ggtggcgggg aagacggaca gggtgacttc tggaagacag tgaagactga     180
aggttttcct ggcttctggg gctcatctgg ctctgattcc ggctccttct ccagggtcaag     240
atccagggtt cagagctact ttcttggggg actactnggg aatcccgttc tcatctgggg      300
gtngaggggg gacggggnaa gggncatgct tgtgaccgag gtttccacc tcggcccgcg      360
accacgctaa ggcccggaatt ncagcacact tggcgggcccg t                               401

```

```

<210> 115
<211> 401
<212> DNA
<213> Homo sapien

```

```

<400> 115
atccctgtaa gtctattaaa tgtaaataat acatacttta caacttctct tagtcggccc      60
ttggcagatt aaatctttgc aaaattccat atgtgctatt gaaaaatgaa ataaaacctc     120
agatgtctga attcttattt caaatacagt tatataatta ttttaaatta caataatacaa     180
tttctgttaa atacaactgt taagggatcc tgagaacaat tataagatta taataatata      240
tacaaactaa cttctgaaat gacatgggtt gtttccttcc caccctccta ccctctcaaa      300
gagtttttgc atttctgtgt cctggttgca aaaggcaaaa gaaaatctaa aaatagtctg      360
tgtgtgtcca cgacatgctc gctcctttga gaatctcaaa c                               401

```

```

<210> 116
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 116
ngattttaatt gnnagcttct ttttaatgga atnnttggtt aaaatgaatt gatgattatg      60
aatatcccta ggaggagtta gcatggannn tgatcatttt cttnngnactc ctttangaca     120
nggaaacagg natcagcatg anggtancan aaaccttatn accnangcgc acganctgac     180
ttcttccaaa gagttgnggt tccgggcagc ggtcattgcc gtgcccattg ctggagggct      240
gattctagtg ntgcttatta tgctggccct gaggatgctt ccaanatgaa aataagangc      300
t                               301

```

```

<210> 117
<211> 383
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(383)

```

<223> n = A,T,C or G

<400> 117

aattgcaact	ggacttttat	tgggcagtta	cnacaacnaa	tgttttcana	aaaatatttg	60
gaaaaaatat	accacttcat	agctaagtct	tacagagaan	aggatttgct	aataaaactt	120
aagttttgaa	aattaagatg	cnggtanagc	ttctgaacta	atgcccacag	ctccaaggaa	180
nacatgtcct	atttagttat	tcaaatacca	gttgagggca	ttgtgattaa	gcaaacaata	240
tatttgttan	aactttgntt	ttaaattact	gntncttgac	attacttata	aaggagnctc	300
taactttcga	tttctaaaac	tatgtaatac	aaaagtatan	ntttcccat	tttgataaaa	360
gggcnanga	tactgantag	gaa				383

<210> 118

<211> 301

<212> DNA

<213> Homo sapien

<400> 118

ctgctagaat	cactgccgct	gtgctttcgt	ggaaatgaca	gttccttggt	ttttttgttt	60
ctgtttttgt	tttacattag	tcattggacc	acagccattc	aggaactacc	ccctgcccc	120
caaagaaatg	aacagttgta	gggagacca	gcagcacctt	tcctccacac	accttcattt	180
tgaagttcgg	gtttttgtgt	taagttaatc	tgtacattct	gtttgccatt	gttacttgta	240
ctatacatct	gtatatagtg	tacggcaaaa	gagtattaat	ccactatctc	tagtgcttga	300
c						301

<210> 119

<211> 401

<212> DNA

<213> Homo sapien

<400> 119

taaggacatg	gacccccggc	tgattgcatg	gaaaggaggg	gcagtgttgg	cttgtttgga	60
tacaacacag	gaactotgga	tttatcagcg	agagtggcag	cgctttggtg	tccgcatgtt	120
acgagagcgg	gctgcgtttg	tgtggtgaat	ggggaggaaa	tgctactgcc	gaagaccaa	180
aacaagcttc	ttggtataaa	agactcttac	agaatatgtg	tattgtaatt	tattgatctg	240
gatgcttaag	tgctatggac	agtaaataaa	tttgaacttt	atgtttgagg	acatgacatt	300
gggtttgaaa	atataaactg	cttttgagca	gtttaagtca	gggcatttga	gaataaaaata	360
ggaactttct	cttcagtttg	taaaactctc	ttgcctcttc	t		401

<210> 120

<211> 301

<212> DNA

<213> Homo sapien

<400> 120

tccagagata	ccacagtcaa	acctggagcc	aaaaaggaca	caaaggactc	tcgacccaaa	60
ctgccccaga	ccctctccag	aggttggggt	gaccaactca	tctggactca	gacatatgaa	120
gaagctctat	ataaatccaa	gacaagcaac	aaacccttga	tgattattca	tcacttgggt	180
gagtgcccac	acagtcaagc	tttaaagaaa	gtgtttgctg	aaaataaaga	aatccagaaa	240
ttggcagagc	agtttgtcct	cctcaatctg	gtttatgaaa	caactgacaa	acacctttct	300
c						301

<210> 121

<211> 2691

<212> DNA

<213> Homo sapien

WO 00/37643

PCT/US99/30909

37

<400> 121

gcttgcccg	cggtcgctag	ctcgctcggt	gcgcgtcgtc	ccgctccatg	gcgctcttcg	60
tgcggctgct	ggctctcgcc	ctggctctgg	ccctgggccc	cgccgcgacc	ctggcggggtc	120
ccgccaagtc	gccctaccag	ctggtgctgc	agcacagcag	gctccggggc	cgccagcacg	180
gccccaaagt	gtgtgctgtg	cagaaggtta	ttggcactaa	taggaagtac	ttcaccaact	240
gcaagcagt	gtaccaaagg	aaaatctgtg	gcaaatcaac	agtcattcagc	tacgagtgtc	300
gtcctggata	tgaaaagggtc	cctggggaga	agggtgtgct	agcagcccta	ccactctcaa	360
acctttacga	gaccttggga	gtcgttggat	ccaccaccac	tcagctgtac	acggaccgca	420
cggagaagct	gaggcctgag	atggaggggc	ccggcagctt	caccatcttc	gccccatgca	480
acgaggcctg	ggcctccttg	ccagctgaag	tgctggactc	cctgggtcagc	aatgtcaaca	540
ttgagctgct	caatgccctc	cgctaccata	tggtgggcag	gcgagtcctg	actgatgagc	600
tgaaacacgg	catgacctc	acctctatgt	accagaattc	caacatccag	atccaccact	660
atcctaattg	gattgtaact	gtgaactgtg	cccggtcctt	gaaagccgac	caccatgcaa	720
ccaacgggg	ggtgcacctc	atcgataagg	tcattctccac	catcaccaac	aacatccagc	780
agatcattga	gatcgaggac	acctttgaga	cccttcgggc	tgctgtggct	gcacagggc	840
tcaacacgat	gcttgaaagt	aacggccagt	acacgctttt	ggccccgacc	aatgaggcct	900
tcgagaagat	ccctagttag	actttgaacc	gtatcctggg	cgacccagaa	gccctgagag	960
acctgctgaa	caaccacatc	ttgaagtcag	ctatgtgtgc	tgaagccatc	gttgcggggc	1020
tgtctgtaga	gaccttggag	ggcacgacac	tggaggtggg	ctgcagcggg	gacatgctca	1080
ctatcaacgg	gaaggcgatc	atctccaata	aagacatcct	agccaccaac	ggggtgatcc	1140
actacattga	tgagctactc	atccagactc	cagccaagac	actatttgaa	ttggctgcag	1200
agtctgatgt	gtccacagcc	attgaccttt	tcagacaagc	cggcctcggc	aatcatctct	1260
ctggaagtga	gcgggtgacc	ctcctggctc	ccctgaattc	tgtattcaaa	gatggaacct	1320
ctccaattga	tgcccataca	aggaatttgc	ttcggaacca	cataattaaa	gaccagctgg	1380
cctctaagta	tctgtaccat	ggacagaccc	tggaaactct	gggcggcaaa	aaactgagag	1440
tttttgttta	tcgtaatagc	ctctgcatac	agaacagctg	catcgcgggc	cacgacaaga	1500
gggggaggta	cgggaccctg	ttcacgatgg	accgggtgct	gaccccccca	atggggactg	1560
tcatggatgt	cctgaaggga	gacaatcgct	ttagcatgct	ggtagctgcc	atccagctctg	1620
caggactgac	ggagaccctc	aaccgggaag	gagtctacac	agtccttgct	cccacaaatg	1680
aagccttccg	agccctgcca	ccaagagaac	ggagcagact	cttggggagat	gccaaggaac	1740
ttgccaacat	cctgaaatac	cacattggtg	atgaaatcct	ggttagcgga	ggcatcgggg	1800
ccctggtgcg	gctaaagtct	ctccaagggt	acaagctgga	agtcagcttg	aaaaacaatg	1860
tggtgagtgt	caacaaggag	cctgttgccg	agcctgacat	catggccaca	aatggcgtgg	1920
tccatgtcat	caccaatgtt	ctgcagcctc	cagccaacag	acctcaggaa	agaggggatg	1980
aacttgacga	ctctgcgctt	gagatcttca	aacaagcatc	agcgttttcc	agggtctccc	2040
agaggtctgt	gcgactagcc	cctgtctatc	aaaagttatt	agagaggatg	aagcattagc	2100
ttgaagcact	acaggaggaa	tgcaaccacg	cagctctccg	ccaatttctc	tcagatttcc	2160
acagagactg	tttgaatgtt	ttcaaaaacca	agtatcacac	tttaatgtac	atgggcccga	2220
ccataatgag	atgtgagcct	tgtgcatgtg	gggyaggagg	gagagagatg	tactttttaa	2280
atcatgttcc	ccctaaacat	ggctgttaac	ccactgcatg	cagaaacttg	gatgtcactg	2340
ctgcacattc	acttccagag	aggacctatc	ccaaatgtgg	aattgactgc	ctatgccaaag	2400
tccttggaata	aggagcttca	gtattgtggg	gctcataaaa	catgaatcaa	gcaatccagc	2460
ctcatgggaa	gtcctggcac	agtttttgta	aagcccttgc	acagctggag	aaatggcatc	2520
attataagct	atgagttgaa	atgttctgtc	aaatgtgtct	cacatctaca	cgtggcttgg	2580
aggcttttat	ggggccctgt	ccaggtagaa	aagaaatggt	atgtagagct	tagatttccc	2640
tattgtgaca	gagccatggt	gtgtttgtaa	taataaaacc	aaagaaacat	a	2691

<210> 122

<211> 683

<212> PRT

<213> Homo sapien

<400> 122

Met Ala Leu Phe Val Arg Leu Leu Ala Leu Ala Leu Ala Leu

1	5	10	15
Gly Pro Ala	Ala Thr Leu	Ala Gly Pro	Ala Lys Ser Pro Tyr Gln Leu
	20	25	30
Val Leu Gln	His Ser Arg Leu	Arg Gly Arg Gln	His Gly Pro Asn Val
	35	40	45
Cys Ala Val	Gln Lys Val Ile	Gly Thr Asn Arg	Lys Tyr Phe Thr Asn
	50	55	60
Cys Lys Gln	Trp Tyr Gln	Arg Lys Ile Cys	Gly Lys Ser Thr Val Ile
	65	70	75
Ser Tyr Glu	Cys Cys Pro	Gly Tyr Glu	Lys Val Pro Gly Glu Lys Gly
	85	90	95
Cys Pro Ala	Ala Leu Pro	Leu Ser Asn Leu	Tyr Glu Thr Leu Gly Val
	100	105	110
Val Gly Ser	Thr Thr Thr	Gln Leu Tyr	Thr Asp Arg Thr Glu Lys Leu
	115	120	125
Arg Pro Glu	Met Glu Gly	Pro Gly Ser	Phe Thr Ile Phe Ala Pro Ser
	130	135	140
Asn Glu Ala	Trp Ala Ser	Leu Pro Ala	Glu Val Leu Asp Ser Leu Val
	145	150	155
Ser Asn Val	Asn Ile Glu	Leu Leu Asn	Ala Leu Arg Tyr His Met Val
	165	170	175
Gly Arg Arg	Val Leu Thr	Asp Glu Leu	Lys His Gly Met Thr Leu Thr
	180	185	190
Ser Met Tyr	Gln Asn Ser	Asn Ile Gln	Ile His His Tyr Pro Asn Gly
	195	200	205
Ile Val Thr	Val Asn Cys	Ala Arg Leu	Leu Lys Ala Asp His His Ala
	210	215	220
Thr Asn Gly	Val Val His	Leu Ile Asp	Lys Val Ile Ser Thr Ile Thr
	225	230	235
Asn Asn Ile	Gln Gln Ile	Ile Glu Ile	Glu Asp Thr Phe Glu Thr Leu
	245	250	255
Arg Ala Ala	Val Ala Ala	Ser Gly Leu	Asn Thr Met Leu Glu Gly Asn
	260	265	270
Gly Gln Tyr	Thr Leu Leu	Ala Pro Thr	Asn Glu Ala Phe Glu Lys Ile
	275	280	285
Pro Ser Glu	Thr Leu Asn	Arg Ile Leu	Gly Asp Pro Glu Ala Leu Arg
	290	295	300
Asp Leu Leu	Asn Asn His	Ile Leu Lys	Ser Ala Met Cys Ala Glu Ala
	305	310	315
Ile Val Ala	Gly Leu Ser	Val Glu Thr	Leu Glu Gly Thr Thr Leu Glu
	325	330	335
Val Gly Cys	Ser Gly Asp	Met Leu Thr	Ile Asn Gly Lys Ala Ile Ile
	340	345	350
Ser Asn Lys	Asp Ile Leu	Ala Thr Asn	Gly Val Ile His Tyr Ile Asp
	355	360	365
Glu Leu Leu	Ile Pro Asp	Ser Ala Lys	Thr Leu Phe Glu Leu Ala Ala
	370	375	380
Glu Ser Asp	Val Ser Thr	Ala Ile Asp	Leu Phe Arg Gln Ala Gly Leu
	385	390	395
Gly Asn His	Leu Ser Gly	Ser Glu Arg	Leu Thr Leu Leu Ala Pro Leu
	405	410	415
Asn Ser Val	Phe Lys Asp	Gly Thr Pro	Pro Ile Asp Ala His Thr Arg
	420	425	430
Asn Leu Leu	Arg Asn His	Ile Ile Lys	Asp Gln Leu Ala Ser Lys Tyr
	435	440	445

PCT/US99/30909

Leu	Tyr	His	Gly	Gln	Thr	Leu	Glu	Thr	Leu	Gly	Gly	Lys	Lys	Leu	Arg
450						455					460				
Val	Phe	Val	Tyr	Arg	Asn	Ser	Leu	Cys	Ile	Glu	Asn	Ser	Cys	Ile	Ala
465					470					475					480
Ala	His	Asp	Lys	Arg	Gly	Arg	Tyr	Gly	Thr	Leu	Phe	Thr	Met	Asp	Arg
				485					490					495	
Val	Leu	Thr	Pro	Pro	Met	Gly	Thr	Val	Met	Asp	Val	Leu	Lys	Gly	Asp
			500					505					510		
Asn	Arg	Phe	Ser	Met	Leu	Val	Ala	Ile	Gln	Ser	Ala	Gly	Leu	Thr	
		515					520				525				
Glu	Thr	Leu	Asn	Arg	Glu	Gly	Val	Tyr	Thr	Val	Phe	Ala	Pro	Thr	Asn
		530				535					540				
Glu	Ala	Phe	Arg	Ala	Leu	Pro	Pro	Arg	Glu	Arg	Ser	Arg	Leu	Leu	Gly
545					550					555					560
Asp	Ala	Lys	Glu	Leu	Ala	Asn	Ile	Leu	Lys	Tyr	His	Ile	Gly	Asp	Glu
				565					570					575	
Ile	Leu	Val	Ser	Gly	Gly	Ile	Gly	Ala	Leu	Val	Arg	Leu	Lys	Ser	Leu
			580					585					590		
Gln	Gly	Asp	Lys	Leu	Glu	Val	Ser	Leu	Lys	Asn	Asn	Val	Val	Ser	Val
		595					600					605			
Asn	Lys	Glu	Pro	Val	Ala	Glu	Pro	Asp	Ile	Met	Ala	Thr	Asn	Gly	Val
		610					615				620				
Val	His	Val	Ile	Thr	Asn	Val	Leu	Gln	Pro	Pro	Ala	Asn	Arg	Pro	Gln
625					630					635					640
Glu	Arg	Gly	Asp	Glu	Leu	Ala	Asp	Ser	Ala	Leu	Glu	Ile	Phe	Lys	Gln
				645					650					655	
Ala	Ser	Ala	Phe	Ser	Arg	Ala	Ser	Gln	Arg	Ser	Val	Arg	Leu	Ala	Pro
			660					665					670		
Val	Tyr	Gln	Lys	Leu	Leu	Glu	Arg	Met	Lys	His					
		675					680								

```
<210> 123
<211> 1205
<212> DNA
<213> Homo sapien
```

<400> 123

cagatcagca	gagggacagg	aatcattcgg	ccactgttca	gacgggagcc	acacccttct	60
ccaatccaag	cctggcccca	gaagatcaca	aagagccaaa	gaaactggca	ggtgtccacg	120
cgctccaggc	cagtgaattg	gttgtcactt	actttttctg	tggggaagaa	attccatacc	180
ggaggatgct	gaaggctcag	agcttgaccc	tgggccactt	taaagagcag	ctcagcaaaa	240
agggaaatta	taggtattac	ttcaaaaaag	caagcgatga	gtttgcctgt	ggagcggtgt	300
ttgaggagat	ctgggaggat	gagacggtgc	tcccgatgta	tgaaggccgg	attctgggca	360
aagtggagcg	gatcgattga	gccctgcggt	ctggctttgg	tgaactgttg	gagcccgaag	420
ctcttgtgaa	ctgtcttggc	tgtgagcaac	tgcgacaaaa	cattttgaag	gaaaattaaa	480
ccaatgaaga	agacaaagtc	taaggaagaa	tcggccagtg	ggccttcggg	agggcggggg	540
gaggttgatt	ttcatgattc	atgagctggg	tactgactga	gataagaaaa	gcttgaacta	600
tttattaaaa	acatgaccac	tcttggctat	tgaagatgct	gcttgtattt	gagagactgc	660
catacataat	atatgacttc	ctagggatct	gaaatccata	aactaagaga	aactgtgtat	720
agcttacctg	aacaggaaatc	cttactgata	tttatagaac	agttgatttc	ccccatcccc	780
agtttatgga	tatgctgctt	taaaacttga	agggggagac	aggaagtttt	aattgttctg	840
actaaactta	ggagttgagc	taggagtgcg	ttcatggttt	cttcactaac	agaggaatta	900
tgctttgcac	tacgtccctc	caagtgaaga	cagactgttt	tagacagact	ttttaaaattg	960
gtgccctacc	attgacacat	gcagaaattg	gtgcgttttg	tttttttttc	ctatgctgct	1020
ctgttttgtc	ttaaaggctc	tgaggattga	ccatgttgcg	tcatcatcaa	cattttgggg	1080

WO 00/37643

PCT/US99/30909

40

gttgtgttgg atgggatgat ctgttcgaga gggagaggca gggaaccctg ctccttcggg	1140
ccccagggtg atcctgtgac tgaggctccc cctcatgtag cctccccagg cccagggccc	1200
tgagg	1205

<210> 124
<211> 583
<212> DNA
<213> Homo sapien

<400> 124	
ccaagaagca gtggccttat tgcaccccaa accacgcctc ttgaccaggc tgcctccctt	60
gtggcagca... cggcacagct aattctactc acagtgcctt taagtgaata ttgtcgagaa	120
agaggcaacca ggaagccgtc ctggcgccctg gcagtcctgt ggacgggatg gttctggctg	180
tttgagattc tcaaaggagc gagcatgtcg tggacacaca cagactattt ttagattttc	240
ttttgccttt tgcaaccagg aacagcaaat gcaaaaactc tttgagaggg taggagggtg	300
ggaaggaaac aacctgtca ttccagaagt tagttgtat atattattat aatcttataa	360
ttgttctcag aatcccttaa cagttgtatt taacagaaat tgtatattgt aatttaaaat	420
aattatataa ctgtatttga aataagaatt cagacatctg aggttttatt tcatttttca	480
atagcacata tggaattttg caaagattta atctgccaaag ggccgactaa gagaagttgt	540
aaagtatgta ttatttacat ttaatagact tacagggata agg	583

<210> 125
<211> 783
<212> DNA
<213> Homo sapien

<400> 125	
tcaaccatac atactgcttc cactagctaa taccaaattgc aggttctcag atccagacaa	60
atggaggaaa agaacattta tgcttcctgt tcagaaagcc aagtcgtagt ttggccctt	120
cctttctcta aagtttatcc ccaaaaacag gtagcattcc tgattgggca gagaagagga	180
tattttcagc ccacatctgc tgcaggtatg tcattttctc ccatcttcac tgtgactagt	240
aaagatctca ccacttctct ttggaatttc caactttgct tgtgattgaa tgtcacttcg	300
tgaatttcta ttatgtcaga tcacttgga ttgctcttcc atatgcacaa agttgccagg	360
cactgttgcg ctgtcgggcc cactggaatc cacgggggtg aaacaaattc aattatgctt	420
ttacagatcc tgctcaaaaa aggtttcaac tgcttaacca agtacagctc attcttcac	480
cttcttactc tgcaacaaaa ccaagtgcct catactacag gtaggtgccg agaaattccg	540
cagcagaaaa tccaaaatca ttcttgaaac ctcttgcta acaaaagtcc tttttttctc	600
caaacagcat ataaaatgat caagtcttga aagagaaaag aagcaaagta gcaatacat	660
caacaattca ctatcagaaa cacataaaat cccagagaga gagaaggcag tatctctgaa	720
tcatggatgg acttggaac... ttcggaagga ttccgagtg ttcctttcag aaagacaatt	780
ctg	783

<210> 126
<211> 604
<212> DNA
<213> Homo sapien

<400> 126	
cctgctagaa tcactgccgc tgtgctttcg tggaaatgac agttccttgt tttttttgtt	60
tctgtttttg ttttacatta gtcattggac cacagccatt caggaactac cccctgcccc	120
acaaagaaat gaacagttgt agggagaccc agcagcacct ttctccaca cacttcatt	180
ttgaagttcg ggtttttgtg ttaaagttaa tctgtacatt ctgtttgcc tttgtacttg	240
tactatacat ctgtatatag tgtacggcaa aagagtatta atccactatc tctagtgtt	300
gactttaaat cagtacagta cctgtacctg cacggtcacc cgctccgtgt gtcgccctat	360
attgagggct caagctttcc cttgtttttt gaaaggggtt tatgtataaa tatattttat	420

WO 00/37643

PCT/US99/30909

41

```
gccttttttat tacaagtctt gtactcaatg acttttgtca tgacattttg ttctacttat 480
actgtaaatt atgcattata aagagttcat ttaaggaaaa ttacttggtg caataattat 540
tgtaattaav agatgtagcc tttattaaaa ttttatattt ttcaaaaaaa aaaaaaaaaa 600
aaaa 604
```

```
<210> 127
<211> 417
<212> DNA
<213> Homo sapien
```

```
<400> 127
ctgagcctct gtcaccagag aaggctgagg ccccaatggc acacctcaga aacctacacc 60
ccgaggctgg acggctggac tcctgagcac aagctccctc tcgcaccctt tgccagacag 120
tttgtctcca atttcaaaact gacctaaaggc tcttactcct ggattttttg tttttaaac 180
ttctcccagc cagtcttcgg gagggcatga ttagagaagt gctcctttgc tgatggagga 240
ggggacctaa ggaagaagggt ggatcccagg tgccctctct ctaattgatc cccccacct 300
agtttctctt gcctctcttc cttctaccag gtcattgttt ttactctctg ccccttctgc 360
ctcttagcat ttcaaaaact gtagagtgcg ccccatagtg gacattttta gtccagg 417
```

```
<210> 128
<211> 657
<212> DNA
<213> Homo sapien
```

```
<400> 128
ccacactgaa atgcagttta atgtggaaac ttttctaaat acatattgta gcatctttgg 60
acatcaacgt gtggcctgaa atttttatta ttgttcctc ttctcctcca ttaaaaaaa 120
aatctccttg tggatatttag tcatttacca ttaacacata ttatggctta aaaaggcca 180
tcctctcctt ttctgagctg gatttcttca cgtcacctt tgatgcatgg ccttagctgg 240
ttactttgcc ttggtttggg catgaacatt ggggttagtg gcctggcaac ttgaatgcat 300
atggaaagaa caatgccaag tgatctgaca taatacaaat tccgaagtga cattcaatca 360
caagcaaagt tggaaattcc aaagagaagt ggtgagatct ttactagtca cagtgaagat 420
gggagaaaat gacatacctg cagcagatgt gggctgaaaa taccctcttc tctgccaat 480
caggaaatgt acctgttttt gggaataaac ttttagagaaa ggaaggcca aaactacgac 540
ttggctttct gaaacggaag cataaatgtt cttttcctcc atttgtctgg atctgagaac 600
ctgcatttgg tattagctag tggaagcagt atgtatggtt gaagtgcatt gctgcag 657
```

```
<210> 129
<211> 1220
<212> DNA
<213> Homo sapien
```

```
<400> 129
cgcgtgctcg gctcacacca acaaggcaag ccaaaggcgc cctccccag agggatccct 60
aacgtgcca gcatgtagat tctggactaa cagacaacat acattcaccg ctggtcacc 120
agatcctcat tcaaacccac tgctggcaca tccctttcct tactttgcc tgtgctacca 180
gccacggaag gagcctctct tgtttttct ataaaatggg taggcaggag aaaagcagg 240
gccctaagat tgctctaagg ccagcatgt ggttacagtt ctctgacttg cagaacctgc 300
cagggtgatg gctacaagtt atcctcgtgc tgatctgtct cactactaag ttaatggaga 360
agacagaaag gtaaaaatca cgtgtagcaa gaacaactct tatttcacaa actcaggtat 420
gaaacgaaac gcctgtcctt catggaactg ctttttagctc ctgtcttttc aaaatggcag 480
aggagttcc tacacacact tttccctgg aggccaagg ctaggggtag aaaggggagg 540
ggtgggcta ccaggtagca gttgacaacc caaggtcaga ggagtggccc tcagtgtcat 600
ctgtccacag tgatacctgc caagatgacc actgaccac atctggtctt agtcattggt 660
ctcctcagat ttctggggcc acctgcaagc cccattccat tcctacagat ctctcagcca 720
```

WO 00/37643

PCT/US99/30909

42

cctgtaagtc	ctttgtgaag	atgtgggtga	cacaggggga	caggaaaacc	catttctcaa	780
cccagatcca	tgtctccact	gcttctactc	tgggttggga	ttcaggaaga	caggcacagt	840
cctctctgtt	catagaaaca	cctgccagtg	tcaaggattc	cagtcagggtg	tctatcccaa	900
ctggtcaggg	agagaagggc	agacccattc	tcaaagacca	ccatgtccaa	ggtctgacag	960
ctccccactg	gctgccccca	caggggcttt	aggctgggtc	gggtcatggg	gaagcgtccc	1020
tcttatcgct	ggctctgtgt	ctcctggatt	tgggtatctat	gttggtacga	ctcctggcct	1080
tttatctaaa	ggactttggc	ttttgtaaat	cacaagccaa	taatagactt	ttttctcccc	1140
ctctgttttt	tgtctgtgtc	tctctgcctt	gagactgcct	tgagacagtg	cttgccttga	1200
gagagtgagc	caattaacag					1220

<210> 130

<211> 1274

<212> DNA

<213> Homo sapien

<400> 130

ccatatgagt	ttgccatctc	catggatg	atttcaatgc	cttcagggta	atcattctct	50
ccccaaagac	tgccccaggg	gtcatcactc	ctgtgacgaa	atgagggctg	gattgaagat	120
gttctgtctg	gcacccccct	ggctcatctt	ggggctctcag	aagagccata	atcatgacca	180
ttctcagcat	ctgaataatc	aggttctctc	caagtgtctg	gcaagtctctg	attgtcctca	240
gcactgggat	agtctggctc	ccccaaaaag	gggtggagagt	taggttgaat	gtcagcgctc	300
ggataatcag	gcttccccag	agagtctgcg	tatygattga	ttctaaaact	tgtatgtctc	360
agattctttc	tggatcctgg	atgggtcaaa	ttggctctgg	gtccaggatg	atcagagttg	420
ctctgagctc	cagggtagtc	cggttctaa	gagccaaaat	gatctggatg	tggtctggag	480
cctgcatagt	ttccactgct	gctggagcct	gcaaaatcag	gatttcgttg	agatccaggg	540
tagtctgggt	gtctggatga	tgtctgggtg	taggyatgac	tctgaaatc	actataatct	600
ggctctggta	gagaggtagg	atgggtctgg	cttgttctag	aggctgcaga	gtatgcattg	660
cttctgggtg	cagaatagtc	tggattactc	agagatctag	gataatttgg	ttctgccaga	720
gaccacagga	agtctggacg	tgttctggag	gctacagagt	atggattgct	cctgggtgccg	780
gggtaatctg	gattgttcag	aggacctgga	acatctggat	aaccttgagt	tttcaaatac	840
ccctgcgtac	ggttctgaga	ccctgaatag	tcagggtaat	ctgggtcttc	ctcagaccag	900
ttattcctgt	agtaggcaga	catggttgga	tggactcttc	accctggagt	ggtaaaactgt	960
cccagcattt	gcaattactc	agggatcttt	ttttttcac	ttttttgcc	ttattgtctc	1020
tgttttgttc	caagtagatg	caaatgttgt	gcaaaccaac	ttgatcttaa	gatgttggtt	1080
agaacactgg	agtcacgtgt	ccatgggtcc	ttcaggctgg	cttttgatgg	gagctgggat	1140
gcagatgatt	tacggagggt	tataatctgt	gatgctggtc	tgaagtctga	atattccaag	1200
ttgctgactg	caggcagagc	ctcatgtcct	cctggcgctc	ctgttgccgc	tgcttgccgc	1260
ggccctcggg	tcga					1274

<210> 131

<211> 554

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(554)

<223> n = A,T,C or G

<400> 131

ctgtaattct	gccttttcta	ccttcattcc	atccttctct	tgcccagata	aagkccagca	60
gaaattctct	ctttctacct	ctctgggact	ctgagacagg	aaatcttcaa	ggaggagttt	120
ttccctcccc	actattctta	ttctcaacct	ccagaggaa	caaggctgct	gtaccacact	180
cagggcagag	actccacact	atagtgggaa	agcttcaggg	accctcctt	ttagtctca	240
gggctcacct	atgctactgg	tccttttggc	aaaaaaggaa	aatgatagag	ccaggggtgc	300

43

<210> 135

WO 00/37643

PCT/US99/30909

44

<211> 414

<212> DNA

<213> Homo sapien

<400> 135

```
ctccagcctg gctatatccg gtcccgttat aacctgggca tcagctgcat caacctcggg      60
gtccaccggg aggtctgtga gcactttctg gaggccctga acatgcagag gaaaagccgg      120
ggcccccggg gtgaaggagg tgccatgtcg gagaacatct ggagcaccct gcgtttggca      180
ttgtctatgt taggccagag cgatgcctat ggggcagccg acgcgcggga tctgtccacc      240
ctcctaacta tgtttggcct gcccagtgta cagtgggacg ggctgccttg tgagtgtcca      300
cctggggatt aaatatgtct tcaacaaggg aggcctggct tctacaatgg tttaggtaaa      360
ggggcctttg aagtagttct ggcagggtt gc ttcaca caacacaaga gccca      414
```

<210> 136

<211> 461

<212> DNA

<213> Homo sapien

<400> 136

```
gaagtgatta ataggtttat ttgcatatac acagagaaga gtcagcattg ttgggtgaga      60
agaggcaggc tgtgaggagg taaggcttca gcagaggaag gcaccttgac agacaacacg      120
agactcctat taaatcagca cagttgcaaa cttcacctgc ctcaagccaa cagctcattg      180
aactcatatg tcgattgaga atcatttaca aaaccaggag agaaacaatg ggaagagcaa      240
cggctcttca tccctggacc tgacactcaa aacattatgt acaggatgca ggaacaaaat      300
ctgtctgac agtgccctct cctgctggga aaaacacca tcacggaaga atttggggat      360
taaatatgtc ttcaacaagg gaggcctggc ttctacaatg gtttaggtaa aggggccttt      420
gaagtagttc tggccaggct tgcaatacac acaacacaag a      461
```

<210> 137

<211> 269

<212> DNA

<213> Homo sapien

<400> 137

```
atagcaaatg gacacaaatt acaaatgtgt gtgcgtggga cgaagacatc tttgaaggtc      60
atgagtttgt tagtttaaca tcatatattt gtaatagtga aacctgtact caaaatataa      120
gcagcttgaa actggcttta ccaatcttga aatttgacca caagtgtctt atatatgcag      180
atctaatagt aaatccagaa cttggactcc atcgttaaaa ttatttatgt gtaacattca      240
aatgtgtgca ttaaatatgc ttccacagt      269
```

<210> 138

<211> 452

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (452)

<223> n = A,T,C or G

<400> 138

```
ctccatggga ggcaaaatat agagaattta tgggtgccca ctcttatgta atcactggac      60
taatcttccc tggtaactat gcaacatttg gacagaaagg cacacaaaaa agtttaataa      120
tttcatgtgc caatctggaa aaaaataatt taaatcaaca gaacagacag tacatctaca      180
caaatgagga aagcagaaaa gatacctcac attcatttat ctccaggttc aaagtggctt      240
```

WO 00/37643

PCT/US99/30909

45

```

caatgctaaa gtaaattgtat taacatttgg aaaatacaag acaatttttt tgtttgtttt    300
caattttttt agctctatac aatgattaca acataagaca aaaaaaaaaa aaaaacacaa    360
aaaaacaaaac aaaaaaggag ttcaggactt gttatcagtg tccaagtggc taanaactgg    420
ttcccataac aagcattgaa agttaaggcc cc                                452

```

```

<210> 139
<211> 474
<212> DNA
<213> Homo sapien

```

```

<400> 139
tgtgcctttt tgaggttaca attgaaacag atgtgagcac ctgagagact ttccctgatt    60
atattctctc acaaaccact gtaccatatt accttatttt atcttcttga aattcttatt    120
cattggcttg tttgttgtct ctttgcatta gatatatgta agctccttgg cataaatttg    180
acattggtag gggactgaca ttctaacctg gccaggccc taggagagag ataactccac    240
aaagcagcac atactatctt aggttagcag ggagctaact caccatgtag cagatgaaaa    300
aaaccaaacc cagcactgtg cataaatacc acttgccaag aagtcaggtc ctcggaacc    360
gagaatcaac ctccagcaca acgcagggtg ctgggctctg tccccctta gccaccacct    420
cagcctctcc cctccctctg cccaagtgcc caagagcttg gctctctgtg cttt        474

```

```

<210> 140
<211> 487
<212> DNA
<213> Homo sapien

```

```

<400> 140
cttccctgcc tctgtttcct gagaaacgga ttaatagccc tttatcccc tgcacctcc    60
tgcaggggat ggcactttga gccctctgga gccctcccc tgcagagcct tactctcttc    120
agactttctg aatgtacagt gccgttggtt gggatttggg gactggaagg gaccaaggac    180
actgaccca agctgtcctg cctagcgtcc agcgtcttct aggagggtag ggtctgcctg    240
tcttggtgtg gttggtttgg cctgtttgc tgtgactacc cccccctc cccgaaccga    300
gggacggctg ctttctctc tgcctcagat gccacctgcc ccgcccagc tccccatcag    360
cagcatccag actttcagga agggcagggc cagccagtcc agaaccgcat ccctcagcag    420
ggactgataa gccatctctc ggagggcccc ctaataccca agtggagtct ggttcacacc    480
ctggggg

```

```

<210> 141
<211> 248
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(248)
<223> n = A,T,C or G

```

```

<400> 141
ttaaagatgg ggaaatgagg cctgnaaata gaaaagattt gcctagagtc acacacactg    60
tcagggtcagg tagagtcaaa atcaggcacc ccgactcaca gactgcttca cattgccatc    120
agagattgtc ctgcaacaat attatgttta gttctactgc agaataata ctggatctta    180
ccccctttgc ctgatctggc cacaacttgc ttttccaggt ctttccatta ggctctcttc    240
agctaatt

```

```

<210> 142
<211> 173

```

WO 00/37643

PCT/US99/30909

46

<212> DNA

<213> Homo sapien

<400> 142

tactaagatt	gtccaagcct	ccctctttaa	actttctttc	cccttagagg	aatcattact	60
tcgtattaaa	agtttctact	tccttgtaga	atatctacat	ccaatgggcc	atggcacaaa	120
atttaagtct	agaaagaatc	ttaaaggctc	atcttatagt	aaccagaggc	agg	173

<210> 143

<211> 511

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(511)

<223> n = A,T,C or G

<400> 143

cctcgtcaga	ggggtggttc	ctggtnacct	gtactccacg	gacctcgggtg	aagcaaaagc	60
ttcagggcag	agggaatgag	gcaacccagt	ggcagccccg	ctgggccccg	tggtcctctgc	120
tctcctattg	gacgtagagg	caggggagag	acttctctat	acaaatattc	tcatcacaga	180
agggatgac	cttgctgctc	tgccgtaggg	tttttgatgc	tgagctatgc	tgacatgac	240
gttaacctaa	agaacttgga	ctgagctttt	aaaaaaggac	agcaaacaat	tttataatcc	300
ttaaagtgt	atagacggtt	acactagtgc	agggatttgg	ggaggctctt	tggtgtgga	360
ggctgtcact	tgtatttatt	gtgactctaa	atctttgata	gtaaaacaaa	tgtaaaaaga	420
aatgtttgcc	accagatggg	aatagaagtt	ccaataagca	ggctggaatg	ggtggctata	480
cgttgatatca	cgaggaagtt	ttagactctg	a			511

<210> 144

<211> 190

<212> DNA

<213> Homo sapien

<400> 144

cattcttctg	tcacatgcca	attcagttgt	caatcccatt	gtctatgctt	accggaaccg	60
agacttccgc	tacacttttc	acaaaattat	ctccaggat	cttctctgcc	aagcagatgt	120
caagagtggg	aatggtcagg	ctggggtaca	gcctgctctc	ggtgtgggcc	tatgatctag	180
gctctcgctt						190

<210> 145

<211> 169

<212> DNA

<213> Homo sapien

<400> 145

gatgtgggta	tctcctcaga	tgccagttt	gccctctcag	gctcctggga	tggaaccttg	60
cgctctggg	atctcacaac	gggcaccacc	acgaggcgat	ttgtgggcca	taccaaggat	120
gtgctgagt	tgcccttctc	ctctgacaac	cggcagattg	tctctggat		169

<210> 146

<211> 511

<212> DNA

<213> Homo sapien

WO 00/37643

PCT/US99/30909

47

<400> 146

atctagagaa	gatttgggaa	acacatgata	gctatgggta	aatacttaac	agggcaatca	60
caggggaagat	gactagattt	cctaacatcc	atgagtga	tttatagaag	tatactctct	120
gacttgatat	aaaggaagat	tttaaaaaac	atgactgttc	aggagtgttc	aagtagggtc	180
agatgaccag	tgattgggaa	tacttcgtaa	gcaggagcaa	gtaagatctg	agccactgtt	240
ctatcggtag	ggtgtctgtg	gtattccttg	gtcaaagaag	tactctaagc	aacttcagtc	300
tcacgaatta	ctatcaccct	cgtgggcata	catgatgggt	accctaaaga	ggaagtttca	360
gaaggcagta	atattggatc	ctggaatagt	cagacaggag	ccttcattgca	gatacccttt	420
tcagttctcc	atacaccat	tcacaagtgg	tcacaaaaac	accagtagc	tttacttggc	480
tttaccact	taacaatatg	ctcaatatga	g			511

<210> 147

<211> 421

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(421)

<223> n = A,T,C or G

<400> 147

gaccagttga	gttcttcctg	gctattgtat	aatccacagc	cacactgtga	aagcaaatct	60
ggccagttag	caacacagg	agaatctgcc	tgaactgacc	aaagggtgcc	atacttcattg	120
tcagttagaa	tttcacctcc	atcatgttct	aaagagccaa	caacagattc	tagggcactg	180
caaatgctt	cagcaattaa	ttgaagttct	gtttgagtac	attcatcatc	tttgagaatg	240
ctttctgggt	cgttgtgtgt	cttgtgtctg	atatatgcag	ccaaatgagt	ttcagtacag	300
ccacctccca	acaaagccca	tgggttcctg	agtgttaact	gcaggacatg	cagtgccgtc	360
tgacacgtga	gcttcagctc	atcccangca	gtgtcatctc	tggtgcagag	aagccaagct	420
g						421

<210> 148

<211> 237

<212> DNA

<213> Homo sapien

<400> 148

acacaccact	gttggccttc	catctgggtt	aagtcaactg	tgagttagaa	ccgaagataa	60
cagttttgta	ttcataatgg	ccttttcata	ctccaagtac	ttttgagcac	agagcctctt	120
gcttctgacc	tggcacttgg	aacacagata	tatatatctt	ttgttctgtc	cctgggaaac	180
tgatatttgt	gtaagacaac	caccagatat	tttctcta	aaaatcttct	aaaatta	237

<210> 149

<211> 168

<212> DNA

<213> Homo sapien

<400> 149

agagaaagt	aaagtgaat	aatgtttgaa	gacaataagt	ggtggtgtat	cttgtttcta	60
ataagataaa	ctttttgtc	tttgctttat	cttattagg	agttgtatgt	cagtgtataa	120
aacatactgt	gtggtataac	aggcttaata	aattctttaa	aaggagag		168

<210> 150

<211> 68

<212> DNA

PCT/US99/30909

<213> Homo sapien

<220>

<221> misc feature

$\langle 222 \rangle$ (1) ... (68)

<223> n = A,T,C or G

<400> 150

ggtgggggttt ggcagagatg antttaagtg ctgtggccag aagcgggggg ggggtttggt 60
qgaatttt 68

<210> 151

 $\langle 211 \rangle$ 421

<212> DNA

<213> Homo sapien

<400> 151

aggtgacacg	tattcgggat	gaaagtataa	tagtcattcc	ttcaaccctt	gcatttatgg	60
actctggaaa	tcgaagatcc	acagtgagta	aagatgttcg	tccaaagaca	aaaaatagaa	120
acagctcaac	aaagcgagag	acaaaaaaac	aaaatggcac	tgtggctctg	cctttgaagt	180
ctgggctcca	gcagaggggt	gatcttccca	caggagacga	gacggcctat	gacactctcc	240
agaactgttg	tcagtgccga	attttacttc	ccttgcccat	tctaaatgag	caccaggaga	300
gtgcccagag	gttagctcac	caaaaagaaac	tccagtgggg	ctggtgagat	ggctcagcgg	360
tgaagagcac	ccgactgctc	ttccgaaggt	ccggagtcca	aatcccagca	accacatggt	420
g						421

<210> 152

<211> 507

<212> DNA

<213> Homo sapien

$\langle 220 \rangle$

<221> misc feature

<222> (1) ... (507)

<223> n = A, T, C or G

<400> 152

gaattcggca	cnagctcgtg	cgcgcagggt	nggtccnttt	tttgctccgc	ctcgcacnga	60
cttctacag	ctatcgccag	tgtcggcca	cgtcntcctt	cngaggcctg	ggcggcggct	120
ccgtgcgttn	tgggcggggg	gtcgccttct	ncctccccag	cattcacggg	ggctccggcg	180
gccgcggcgt	atcgtgtcc	tccgcccgct	ntgtgtcctc	gtcctcctcn	ggggcctacg	240
gctngctgct	acngcggctt	cctgaccgct	tccnacgggc	tgctggcnng	caacgagaag	300
ctaaccatgc	agaacctnaa	cnaccgcctg	gcctcctacc	tgncacaagg	gcgcnccttg	360
tagggcgcca	acggcnaagt	agagggtgaag	atccnctact	gggtaccaga	agcagggggc	420
tgggcctcgc	ccgactacag	ccactnctnc	acnaccatgc	agtacctgcn	ggganaagat	480
ttnngggngc	caccatngag	aactgca				507

<210> 153

<211> 513

<212> DNA

<213> Homo sapien

<400> 153

gaattcggca cgaggtggct cagatgtcca ctactgggag tatggtcgaa ttgggaattt 60
tatttgtaaa aagcccatgg tgctgggaca tgaagcttcg ggaacagtcg aaaaagtggg 120

WO 00/37643

PCT/US99/30909

49

```

atcatcggta aagcacctaa aaccagggtga tcgtgttgcc atcgagcctg gtgtccccg      180
agaaaaatgat gaattctgca agatgggccc atacaatctg tcacctcca tcttcttctg      240
tgccgcgccc cccgatgacg ggaacctctg ccccttctat aagcacaatg cagccttttg      300
ttacaagctt cctgacaatg tcacctttga ggaaggcgcc ctgatcgagc cactttctgt      360
ggggatccat gcctgcagga gagggcgagt taccctggga cacaaggctc ttgtgtgtgg      420
agctgggcca atcgggatgg tcactttgct cgtggccaaa gcaatgggag cagctcaagt      480
agtgtgtgact gatctgtctg ctacccgatt gtc                                     513

```

<210> 154

<211> 507

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 154

```

ggcacgagct cgtgccgaat tcggcncgag cagacacaat ggtaagaatg gtgcctgtcc      60
tgctgtctct gctgtgtctt ctgggtcctg ctgtcccca ggagaacca gatggtcgtt      120
actctctgac ctatatctac actgggctgt ccaagcatgt tgaagacgtc cccgcgtttc      180
aggcccttgg ctactcaat gacctccagt tctttagata caacagtaaa gacaggaagt      240
ctcagcccat gggactctgg agacagggtg aaggaatgga ggattggaag caggacagcc      300
aacttcagaa ggccagggag gacatcttta tggagaccct gaaagacatc gtggagtatt      360
acaacgacag taacgggtct cacgtattgc agggaagggt tggttgtgag atcgagaata      420
acagaagcag cggagcattc tggaaatatt actatgatgg aaaggactac attgaattca      480
acaaagaaat cccagcctgg gtccccc                                     507

```

<210> 155

<211> 507

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 155

```

ggcacgagga gacctaaggg ctgagtntcg ggaacaggag aaagctctgt tggccctcca      60
gcagcagtgt gctgagcagg cacaggagca tgaggtggag accaggggcc tgcaggacag      120
ctggctgcag gccaggcag tgctcaagga acgggaccag gagctggaag ctctgcgggc      180
agaaagtcag tcctcccggc atcaggagga ggctgcccgg gccgggctg aggtcttgca      240
ggagggccct ggcaaggctc atgctgccct gcaggggaaa gagcagcatc tcctcgagca      300
ggcagaattg agccgcagtc tggaggccag cactgcaacc ctgcaagcct ccctggatgc      360
ctgccaggca cacagtcggc agctggagga ggctctgagg atacaagaag gtgagatcca      420
ggaccaggat ctccgatacc aggaggatgt gcagcagctg cagcaggcac ttgccagag      480
ggatgaagag ctgagacatc agcagga                                     507

```

<210> 156

<211> 509

<212> DNA

<213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(509)
 <223> n = A,T,C or G

<400> 156
 ggacagagga cagagagaac cctgtngaaa gagcgttacc aggaggtcct ggacaaacag 60
 aggcaagtgg agaatcagct ccaagtgcaa ttaaagcagc ttcagcaaag gagagaagag 120
 gaaatgaaga atcaccagga gatattaaag gctattcagg atgtgacaat aaagcgggaa 180
 gaaacaaaga agaagataga gaaagagaag aaggagtttt tgcagaagga gcaggatctg 240
 aaagctgaaa ttgagaagct ttgtgagaag ggcagaagag aggtgtggga aatggaactg 300
 gatagactca agaatcagga tggcgaaata aataggaaca ttatggaaga gactgaacgg 360
 gcctggaagg cagagatctt atcactagag agccgggag agttactggt actgaaacta 420
 gaagaagcag aaaaagaggc agaattgcac cttacttacc tcaagtcaac tcccccaaca 480
 ctggagacag ttcgttccaa acaggagtg 509

<210> 157
 <211> 507
 <212> DNA
 <213> Homo sapien

<400> 157
 ggacagaggg cagccctcct accggcgcac gtggtgccgc cgctgctgcc tcccgtctgc 60
 cctgaaccca gtgcctgcag ccatggctcc cggccagctc gccttattta gtgtctctga 120
 caaaaccggc cttgtggaat ttgcaagaaa cctgaccgct cttgggtttga atcttggtcgc 180
 ttccggaggg actgcaaaaag ctctcagggg tgctggtctg gcagtcagag atgtctctga 240
 gttgacggga ttctctgaaa tgttgggggg acgtgtgaaa actttgcac ctgcagtcca 300
 tgctggaatc ctgactcgta atattccaga agataatgct gacatggcca gacttgattt 360
 caatcttata agagttgttg cctgcaatct ctatcccttt gtaaagacag tggcttctcc 420
 aggtgtaagt gttgaggagg ctgtggagca aattgacatt ggtggagtaa cttactgag 480
 agctgcagcc aaaaaccacg ctcgagt 507

<210> 158
 <211> 507
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(507)
 <223> n = A,T,C or G

<400> 158
 ggacagagtc gagctgtgcc tattcngtc aatccaagag tgagtaatgt gaagtctgtc 60
 tacaaaaacc acattgatgt cattcattat cggaaaacgg atgcaaaacg tctgcatggc 120
 cttgatgaag aagcagaaca gaaacttttt tcagagaaac gtgtggaatt gcttaaggaa 180
 ctttcagga aaccagacat ttatgagagg cttgcttcag ccttggctcc aagcatttat 240
 gaacatgaag atataaagaa gggaattttg cttcagctct ttggcgggac aaggaaggat 300
 tttagtcaca ctggaagggg caaatctcgg gctgagatca acatcttgct gtgtggcgac 360
 cctggtacca gcaagtccca gctgctgcag tacgtgtaca acctcgtccc caggggccag 420
 tacacgtntg ggaagggtc cagtgcantt ggccctnact cntacgtaat gaaagaccct 480
 gagacaaggn anctggnnct gnnacag 507

<210> 159
 <211> 508

WO 00/37643

PCT/US99/30909

51

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(508)
<223> n = A,T,C or G

<400> 159
ggcacnanaa accaggatta tggtnnggat ccaaagattg ctaatgcaat aatgaaggca 60
gcagatgagg tagctgaagg taaattaaat gatcattttc ctctcgtggt atggcagact 120
ggatcaggaa ctacagacaa tatgaatgta aatgaagtca ttagcaatag agcaattgaa 180
atggttaggag gtgaacttgg cagcaagata cctgtgcac ccaacgatca tgtaataaaa 240
agccagagct caaatgatac ttttcccaca gcaatgcaca ttgctgctgc aatagaagtt 300
catgaagtac tgttaccagg actacagaag ttacatgatg ctcttgatgc aaaatccaaa 360
gagtttgcac agatcatcaa gattggacgt actcatactc aggatgctgt tccacttact 420
cttgggcagg aatttagtgg ttatgttcaa caagtaaaat atgcaatgac aagaataaaa 480
gctgccatgc caagaatcta tgagctcg 508

<210> 160
<211> 508
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(508)
<223> n = A,T,C or G

<400> 160
ggcacgagct tggagcaaag tcactnaag gaattagagg acacacttca ggtaggcac 60
atacaagagt ttgagaagg ttagacagac cacagagttt ctttggagga attaaaaaa 120
gaaaaccaac aaataattaa tcaaatataa gaatctcatg ctgaaattat ccaggaaaaa 180
gaaaaacagt tacaggaatt aaaactcaag gtttctgatt tgtcagacac gagatgcaag 240
ttagaggttg aacttgcgtt gaagggaagca gaaactgatg aaataaaaaat tttgctggaa 300
gaaagcagag cccagragaa ggagaccttg aaatctcttc ttgaacaaga gacagaaaat 360
ttgagaacag aaattagtaa actcaaccaa aagattcagg ataataatga aaattatcag 420
gtgggcttag cagagctaag aactttaatg acaattgaaa aagatcagtg tatttccgag 480
ttaattagta gacatgaaga agaactca 508

<210> 161
<211> 507
<212> DNA
<213> Homo sapien

<400> 161
ggcacgagcg ctaccggcgc ctctctgctg gccactgagc cggagccggc ctgagcagcg 60
ctctcgggtt cagtaccac tggaaggact taggcgctcg cgtggacacc gcaagccctt 120
cagtagcctc ggcccaagag gcctgcttcc cactcgctag ccccgccggg ggtccgtgtc 180
ctgtctcgtt ggccggaccc gggcccgagc ccgagcagta gccggcgcca tgtcgtggt 240
ggycatagac ctgggcttcc agagctgcta cgtcgtgtg gcccgcgccg gcggcatcga 300
gactatcgct aatgagtata gcgaccgctg cacgcccggc tgcatctctt ttggtcttaa 360
gaatcgttca attggagcag cagctaaaag ccaggtaat tctaatagcaa agaacacagt 420
ccaagattt aaaagattcc atggccgagc attctctgat ccatttgtgg aggcagaaaa 480
atctaaccct gcatatgata ttgtgca 507

WO 00/37643

PCT/US99/30909

52

<210> 162
<211> 507
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(507)
<223> n = A,T,C or G

<400> 162
ggcaccgagca gctgtgcacc gacatgntct cagtgtcctg agtaagacca aagaagctgg 60
caagatcctc tctaataatc ccagcaaggg actggccctg ggaattgccca aagcctggga 120
gctctacggc tcaccaaatg ctctggtgct actgattgct caagagaagg aaagaaacat 180
atgtgaccag cgtgccatag agaatgagct actggccagg aacatccatg tgatccgacg 240
aacatttgaa gatattctctg aaaaggggtc tctggacca gaccgaaggc tgtttgtgga 300
tggccaggaa attgctgtgg ttacttccg ggatggctac atgcctcgtc agtacagtct 360
acagaattgg gaagcacgtc tactgctgga gaggtcacat gctgccaagt gccagacat 420
tgccaccag ctggctggga ctaagaaggt gcagcaggag ctaagcaggc cgggcatgct 480
ggagatggtg ctccctggcc agcctga 507

<210> 163
<211> 460
<212> DNA
<213> Homo sapien

<400> 163
ggcaccgagaa ataactttat ttcattgtgg gtcgcggttc ttgtttgtgg atcgtctgtga 60
tcgtcacttg acaatgcaga tcttcgtgaa gactctgact ggtaagacca tcaccctcga 120
ggttgagccc agtgacacca tcgagaatgt caaggcaag atccaagata aggaaggcat 180
ccctcctgac cagcagaggc tgatctttgc tggaaaacag ctggaagatg ggcgcaccct 240
gtctgactac aacatccaga aagagtccac cctgcacctg gtgctccgtc tcagagggtg 300
gatgcaaata ttcgtgaaga cactcactgg caagaccatc acccttgagg tggagcccag 360
tgacaccatc gagaacgtca aagcaaagat ccaggacaag gaaggcattc ctctgacca 420
gcagagggtg atctttgccc gaaagcagct ggaagatggg 460

<210> 164
<211> 462
<212> DNA
<213> Homo sapien

<400> 164
ggcaccgagcc ggatctcatt gccacgcgcc cccgacgacc gcccgacgtg cattcccgat 60
tccttttggt tccaagtcca atatggcaac tctaaaggat cagctgattt ataattctct 120
aaaggaagaa cagaccccc agaataagat tacagttggt ggggttggtg ctgttgccat 180
ggcctgtgcc atcagtatct taatgaagga cttggcagat gaacttgctc ttgttgatgt 240
catcgaagac aaattgaagg gagagatgat ggatctccaa catggcagcc ttttccttag 300
aacaccaaag attgtctctg gcaaagacta taatgtaact gcaaactcca agctggctcat 360
tatcacggct ggggcacgtc agcaagagg agaaagccgt cttaatttgg tccagcgtaa 420
cgtgaacatc tttaaattca tcattcctaa tgttgtaaaa ta 462

<210> 165
<211> 462
<212> DNA

WO 00/37643

PCT/US99/30909

53

<213> Homo sapien

<400> 165

ggcagcagga agccatgagc agcaaagtct ctcgcgacac cctgtacgag gcggtgcggg	60
aagtcctgca cgggaaccag cgcaagcgcc gcaagttcct ggagacggtg gagttgcaga	120
tcagcttgaa gaactatgat ccccagaagg acaagcgctt ctcgggcacc gtcaggctta	180
agtccactcc cgcgccctaag ttctctgtgt gtgtcctggg ggaccagcag cactgtgacg	240
aggctaaggc cgtggatatc cccacatgg acatcgaggc gctgaaaaaa ctcaacaaga	300
ataaaaaact ggtcaagaag ctggccaaga agtatgatgc gtttttgcc tcagagtctc	360
tgatcaagca gattccacga atcctcggcc cagggtttaa taaggcagga aagttccctt	420
ccctgctcac acacaacgaa aacatggtgg ccaaagtgga tg	462

<210> 166

<211> 459

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(459)

<223> n = A,T,C or G

<400> 166

ggcagcagag ggacctgtnt gaatggntcc actagggtnn anntgntctt tacttttaac	60
cantnaaata gacctgcccg tgaanangcg ggcntgacac annaanaaga gaagacccta	120
tggagcttta atttattaat gcanacagna cctaacaac ccacangtcc taaactacca	180
agcctgcatt aaaaatttcg gntggggcna cctcnnagca naacccaacc tccgagcaac	240
tcagtctaag acttcaccag tcaaagctga actactatac tcaattgatc caataacttg	300
accaacagan caagntacc tagggataac ancacaatcc tattctagac cccttatnac	360
caatangntt tacacctcna tngnggaacc aggacatccg atggggcagn cgttattaaa	420
gttngttgnt aacnataaag tctacgtgat ctgaggttag	459

<210> 167

<211> 464

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(464)

<223> n = A,T,C or G

<400> 167

gaattgggac caacganaan cntgcggntc ttnttttgcn tccanngccc agctnattgc	60
tcagacacac atggggaagg tnaaggctcg gagtcaacng atttggtngt attgnagcgt	120
ttggtcacca gngctgcttt taactctggn aaagtggata ttgttgatc naatgacccc	180
tncattgacc tnaactacat ggtttacatg ttccaatatg attccaccca tggcaaatc	240
catngcaccg tnaaggctga gaacgggaag cttgtnatca atggaaatcc catcaccatc	300
tttcangaac ganatccntn caaaaatcaa anttgggggc gatgcttggc cncttgaagt	360
accgttcaan gggaannncc ccactttggc cgntntttnc aanccacccc caatttgggn	420
aaaaaaaaag ggggnntttgg gggggggcct tttanntttt tttt	464

<210> 168

<211> 462

<212> DNA

WO 00/37643

PCT/US99/30909

54

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(462)

<223> n = A,T,C or G

<400> 168

```

ggcacgaggn nnaacctnecg gggctggggc agcacgcctt gngcaancct gcactgcact      60
gaagaccgcg tgccggaagc cgnnggcngc nacatgcagn aactgaacca gctgggcgcg      120
cancagttct cagacctgac agaggtgctt ttacacttcc taactgatcc anantangtg      180
gaaatatnt ntgttnatnt catntgaatn atccancncc aatcatanca nntttnatnt      240
cctcataanc ntgtgagaana gcnnccttnt gnttncanan ggtgctntga anangagtct      300
cacangcaan caggtccaag cggatttntt aactntgggt cttantgang agaaagncac      360
ttacttttct gaaanongga agcagaatgc tcccaccctt gctcgatggg ccatacgtca      420
agactctgat gattaaccag ctttanatat ggacnggaaa tt                          462

```

<210> 169

<211> 460

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(460)

<223> n = A,T,C or G

<400> 169

```

ggcacgaggg acagcagacn agacagtcac agcagccttg acaaaacggt cctggaactc      60
aagntcttnt ncncaaagga ggacagagca nacagcagag accatggant ctncctcggc      120
ccctccccac agatggtgca tcccctggca naggtcctcg ctcacagcct cacttctaac      180
cttctggaac ccgcccacca ctgccaagct cactattgaa tccacgccgt tcaatgnntc      240
ntaggggaag gaggngcttt ctactnttnc acaatctgan ccccttcttn tttggttact      300
ancatggctc tncatgtnaa aatactgtna tggntaacct gtcaaattta taggnantnt      360
gctaattggg aaactnccnn tngtctaccc caggggnccc agattcctnn gttcncataa      420
cnattaatth aaccctaat gncaanccct tngttaaaga                          460

```

<210> 170

<211> 508

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(508)

<223> n = A,T,C or G

<400> 170

```

ggcacgaggg ggatttttag gtggctcngt gtgggtatcag gaataatgtg ggaggccaga      60
ttgaagtcca gccaggaac aatggtaatt gtgggactta agaaagtgtg agtacagctg      120
aatgagccgg ggagcagaaa gtatatgcgt caggtatgag gaagaaaata gattttggaa      180
gttatgagaa atgtagagag tgagttgagc atagtttgtg attttgaggg cctctaacag      240
tattaaagca gcggcagcgg ctgcacacag acatgatggc taggctaaaa caggaagggtc      300
aagttgtttg gacagaaagg ctacaggggt cagtcctggc tcttgtgtaa gaattctgac      360
cacactaacc atgcctagga aggaaaggag ttgttctttt gtaagggtatt gaggtttggg      420

```


WO 00/37643

PCT/US99/30909

55

```

agattaatcg gacacgatca gcagggagag cacctgtgtt tttatgagaa ttatgctgag    480
ataggtaaca gatgaggatg aaatttgg                                         508

```

<210> 171

<211> 507

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 171

```

ggcacgagac cagccactag cgcagntctg agcgatggcc tatgtcccg caccgggcta    60
ccagcccacc tacaaccga cgctgcctta ctaccagccc atcccgggcg ggctcaacgt    120
gggaatgtct gtttacatcc aaggagtggc cagcgagcac atgaagcggg tcttcgtgaa    180
ctttgtggtt gggcaggatc cgggctcaga cgctgccttc cacttcaatc cgcggtttga    240
cggctgggac aaggtqgtct tcaacacgtt gcagggcggg aagtggggca gcgaggagag    300
gaagaggagc atgcccttca aaaagggtgc cgcctttgag ctggtcttca tagtcctggc    360
tgagcactac aaggtggtgg taaatggaaa tcccttctat gagtacgggc accggcttcc    420
cctacagatg gtcacccacc tgcaagtgga tggggatctg caacttcaat caatcaactt    480
catcggaggc cagcccctcc ggcccca                                         507

```

<210> 172

<211> 409

<212> DNA

<213> Homo sapien

<400> 172

```

ggcacgagct ggagtgtctg ctgccacccc ctgcctctct gcagaaatgt ctgtcaccta    60
cgatgactct gtgggagtgg aagtgtccag cgacagcttc tgggagggtg ggaactacaa    120
acggactgtg aagcggattg acgatggcca cgcctgtgt ggtgacctca tgaactgtct    180
gcatgagcgg gcacgcatcg agaaggcgta tgcacagcag ctactgagt gggcccagcg    240
ctggaggcag ctggtagaga agggaccaca gtatgggacc gtggagaagg cctggatagc    300
tgtcatgtct gaagcagaga gggtagtgga actgcacctg gaagtgaagg catcactgat    360
gaatgaagac tttgagaaga tcaagaactg gcagaaggaa gcctttcac                                         409

```

<210> 173

<211> 409

<212> DNA

<213> Homo sapien

<400> 173

```

ggcacgaggg cagctagagg aagagtccaa ggccaagaac gcactggccc acgccctgca    60
gtcagctcgc catgactgtg acctgctgcg ggaacagtat gaagaggagc aggaagccaa    120
ggctgagctg cagagggcca tgtccaaggc caacagcgag gtagccaggt ggaggacgaa    180
atatgagacg gatgccatcc agcgcacaga ggagctggaa gaggccaaga agaagctggc    240
tcagcgtctg caggatgctg aggaacatgt agaagctgtg aattccaaat gcgcttctct    300
tgaaaagacg aagcagcgac ttcagaatga agtggaggac ctcatgattg acgtggagag    360
gtctaattgct gcctgcgctg cgcttgataa gaagcagagg aactttgac                                         409

```

<210> 174

<211> 407

<212> DNA

<213> Homo sapien

<400> 174

ggcacgagcc	ggggcggggc	gcggcgctcc	ggctcgaggc	attcggagct	gcgggagccg	60
ggctggcagg	agcaggatgg	cggcggcggc	ggctgcaggc	gaggcgcgcc	gggtgctggt	120
gtacggcggc	aggggcgctc	tgggttctcg	atgcgtgcag	gcttttcggg	cccgcactg	180
gtgggttgcc	agcgttgatg	tggtagagaa	tgaagaggcc	agcgctagca	tcattgttaa	240
aatgacagac	tcgttcactg	agcaggctga	ccagggtgact	gctgaggttg	gaaagctctt	300
gggtgaagag	aagggtggatg	caattctttg	cgttgctgga	ggatgggccc	ggggcaatgc	360
caaatccaag	tctctcttta	agaactgtga	cctgatgtgg	aagcaga		407

<210> 175

<211> 407

<212> DNA

<213> Homo sapien

<400> 175

ggcacgagct	tgcctgctgg	tcgctagctc	gctcgggtgcg	cgctcgtccc	ctccatggcg	60
ctcttcgtgc	ggctgctggc	tctcgccctg	gctctggccc	tgggccccgc	cgcgaccctg	120
gcgggtcccc	ccaagtcgcc	ctaccagctg	gtgctgcagc	acagcaggct	ccggggccgc	180
cagcacggcc	ccaacgtgtg	tgctgtgcag	aaggttattg	gcactaatag	gaagtacttc	240
accaactgca	agcagtggta	ccaaaggaaa	atctgtggca	aatcaacagt	catcagctac	300
gagtgtgtc	ctggatatga	aaaggtccct	ggggagaagg	gctgtccagc	agccctacca	360
ctctcaaac	tttacgagac	cctgggagtc	gttggatcca	ccaccac		407

<210> 176

<211> 409

<212> DNA

<213> Homo sapien

<400> 176

ggcacgagtg	gtgccaaaac	gggaccatgc	cctcctggag	gagcagagca	agcagcagtc	60
caacgagcac	ctgcgccgcc	agttcgccag	ccaggccaat	gttggtgggc	cctggatcca	120
gaccaagatg	gaggagatcg	ggcgcatctc	cattgagatg	aacgggaccc	tggaggacca	180
gctgagccac	ctgaagcagt	atgaacgcag	catcgtggac	tacaagccca	acctggacct	240
gctggagcag	cagcaccagc	tcacccagga	ggccctcatc	ttcgacaaca	agcacaccaa	300
ctataccatg	gagcacatcc	gcgtgggctg	ggagcagctg	ctcaccacca	ttgcccgcac	360
catcaacgag	gtggagaacc	agatcctcac	ccgcgacgcc	aagggcatc		409

<210> 177

<211> 408

<212> DNA

<213> Homo sapien

<400> 177

ggcacgaggt	ccaggtaact	gcaaaaacaa	tggctcagca	tgaagaactg	atgaagaaaa	60
ctgaaacaat	gaatgtagtt	atggagacca	ataaaatgct	aagagaagag	aaggagcagg	120
tttcaaaaat	ggcatcagtc	cgtcagcatt	tggagaaac	aacacagaaa	gcagaatcac	180
agttgttggg	gtgtaaagca	tcttgggagg	aaagagagag	aatgttaaag	gatgaagttt	240
ccaaatgtgt	atgtcgctgt	gaagatctgg	agaaacaaaa	cagattactt	catgatcaga	300
tcgaaaaatt	aagtgacaag	gtcgttgccct	ctgtgaagga	aggtgtacaa	gttccactga	360
atgtatctct	cagtgaagaa	ggaaaatctc	aagaacaaat	tttggaaa		408

<210> 178

<211> 92

PCT/US99/30909

<212> DNA
<213> Homo sapien

```
ggcacgagaa gaaattaaga gctaaagaca aggagaatga aaatatgggt gcaaagctga 60
acaaaaaaagt taaagagcta gaagaggaga tg 92
```

```
<210> 179
<211> 411
<212> DNA
<213> Homo sapien
```

ggcagcaggga	gacacgccac	ctataccaca	gttctcagaa	tgaattagct	aagttggaat	60
cagaacttaa	gagtctcaaa	gaccagttga	ctgatttaag	taactcttta	gaaaaatgta	120
aggaacaaaa	aggaaacttg	gaagggatca	taaggcagca	agaggctgat	attcaaaatt	180
ctaagttcag	ttatgaacaa	ctggagactg	atcttcaggc	ctccagagaa	ctgaccagta	240
ggctgcatga	agaaataaat	atgaaagagc	aaaagattat	aagcctgctt	tctggcaagg	300
aagaggcaat	ccaagtagct	attgctgaac	tgcgtcagca	acatgataaa	gaaattaaag	360
agctggaaaa	cctgctgtcc	caggaggaag	aggagaatat	tgttttagaa	g	411

```
<210> 180
<211> 411
<212> DNA
<213> Homo sapien
```

ggcacgaggt	tgttcggagc	gggcgagcgg	agttagcagg	gctttactgc	agagcgcgcc	60
gggcactcca	gcgaccgtgg	ggatcagcgt	aggtgagctg	tggccttttg	cgagggtgctg	120
cagccatagc	tacgtgcgtt	cgctacgagg	attgagcgtc	tccaccatc	ttctgtgctt	180
caccatctac	ataatgaatc	ccagtatgaa	gcagaacaa	gaagaaatca	aagagaatat	240
aaagactagt	tctgtcccaa	gaagaactct	gaagatgatt	cagcctttctg	catctggatc	300
tcttgttgga	agagaaatg	agctgtccgc	aggcttgctc	aaaaggaaac	atcggaatga	360
ccacttaaca	tctacaactt	ccagccctgg	ggttattgtc	ccagaatcta		411

```
<210> 181
<211> 411
<212> DNA
<213> Homo sapien
```

ggcacgaggc	gggacagggc	gaagcggcct	gcgcccacgg	agcgcgcgac	actgcccgga	60
agggaccgcc	acccttgccc	cctcagctgc	ccactcgtga	tttcacgcg	cctccgcgcg	120
cgcacgatgc	cctcggccac	cagccacagc	gggagcgcca	gcaagtcgtc	cggaccgccca	180
ccgccgtcgg	gttctctccg	gagtgaggcg	gccgcgggag	ccggggccgc	cgcgcgggct	240
tctcagcacc	ccgcaaccgg	caccggcgct	gtccagaccg	aggccatgaa	gcagattctc	300
ggggtgatcg	acaagaaact	tgggaacctg	gagaagaaaa	agggtaagct	tgatgattac	360
caggaacgaa	tgaacaaagg	ggaaaggcct	aatcaagatc	agctggatgc	c	411

```
<210> 182
<211> 411
<212> DNA
<213> Homo sapien
```

<400> 182

```
ggcacgagcc gacatggagc tgttctctgc gggccgcccgg gtgctggtca ccggggcagg      60
caaaggtata gggcgccgca cgggccaggc gctgcacgcg acggggcgcg ggggtggtggc      120
tgtgagccgg actcaggcgg atcttgacag ccttgctccg gagtgcccgg ggatagaacc      180
cgtgtgctg gacctgggtg actgggaggg caccgagcgg gcgctgggca gcgtggggccc      240
cgtggacctg ctggtgaaca acgccgctgt cgccctgctg cagcccttcc tggaggtcac      300
caaggaggcc tttagacagat cctttgaggt gaacctgcgt gcggtcatcc aggtgtcgca      360
gattgtggcc aggggcttaa tagcccgggg agtcccaggg gccatcgtga a                411
```

<210> 183

<211> 409

<212> DNA

<213> Homo sapien

<400> 183

```
ggcacgagcc tacactctgg ccagagatac cacagtcaaa cctggagcca aaaaggacac      60
aaaggactct cgacccaaac tgcccagac cctctccaga ggttgggggtg accaactcat      120
ctggactcag acatatgaag aagctctata taaatccaag acaagcaaca aacccttgat      180
gattattcat cacttggatg agtgcctca cagtcaagct ttaaagaaag tgtttgctga      240
aaataaagaa atccagaaat tggcagagca gtttgtcttc ctcaatctgg ttatgaaac      300
aactgacaaa cacctttctc ctgatggcca gtatgtcccc aggattatgt ttgttgaccc      360
atctctgaca gtttagagccg atatcactgg aagatattca aatcgtctc                409
```

<210> 184

<211> 410

<212> DNA

<213> Homo sapien

<400> 184

```
ggcacgaggt cattccagca ccaacaggat ccaagccaga ttgattgggc tgcattggcc      60
caagcttgga ttgcccaga agaatgttca ggacagcaaa gcattggtaga acaaccacca      120
ggaatgatgc caaatggaca agaatgtctt acaatggaat ctggtccaaa caatcatggg      180
aatttccaag gggattcaaa cttcaacaga atgtggcaac cagaatgggg aatgcatcag      240
caacccccac accccccacc agatcagcca tggatgccac caacaccagg cccaatggac      300
attgttcttc cttctgaaga cagcaacagt caggacagtg gggaatttgc ccttgacaac      360
aggcatatat ttaaccagaa caatcacaac tttggtggac caccgataa                410
```

<210> 185

<211> 411

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(411)

<223> n = A,T,C or G

<400> 185

```
ggcacgagca cagatgtagt tttctctgcg cgtgtgcgtt ttccctcttc ccccgccctc      60
agggctccac gccaccatgg cgtattaggg gcagcagtcg ctgcggcagc attggccttt      120
gcagcggcgg cagcagcacc aggtcttgca gcggcaaccc ccagcggctt aagccatggc      180
gcttctcacg gcattcagca gcagcgttgc tgtaaccgac aaagacacct tcgaattaag      240
cacattcttc gattccagca aagcaccgca acatgaccga aatgagcttc ctgagcagcg      300
aggtgttggg gggggacttg atgtcccttc tcgaccgcgc ggggttgggg gctgaagaaa      360
gcctangtct cttagatgat tacctggagg tggccaagca cttcaaacct c                411
```

```
<210> 186
<211> 410
<212> DNA
<213> Homo sapien
```

<400> 186						
ggc	acg	agc	t	t	c	60
g	c	a	g	c	a	120
c	a	a	g	a	c	180
g	g	a	t	a	c	240
t	c	c	a	a	c	300
c	g	a	g	g	t	360
a	g	a	c	g	a	410

```
<210> 187
<211> 506
<212> DNA
<213> Homo sapien
```

<400> 187						
ctttcgtggc	tcactccctt	tcct.ctgctg	ccgctcggtc	acgcttgtgc	ccgaaggagg	60
aaacagtgac	agacctggag	actgcagttc	tctat.ccttc	acacagctct	ttcaccatgc	120
ctggatcact	tcctttgaat	gcagaagctt	gctggccaaa	agatgtggga	attgttgccc	180
ttgagatcta	ttttccttct	caatatgttg	atcaagcaga	gttggaaaaa	tatgatggtg	240
tagatgctgg	aaagtatacc	attggcttgg	gccaggccaa	gatgggcttc	tgacagata	300
gagaagatag	taactctctt	tgcattgactg	tggttcagaa	tcttatggag	agaaaataac	360
tttctatgat	ttgcatttgg	cggctgggaag	ttggaacaga	gacaatcatc	gacaaatcaa	420
agtctgtgaa	gactaatttg	atgcagctgt	ttgaagaytc	tgggaataca	gatatagaag	480
gaatcgacac	aactaatgca	tgctat				506

```
<210> 188
<211> 506
<212> DNA
<213> Homo sapien
```

<400> 188							
gccacagagg	cggcggagag	atggccttca	gcggttccca	ggctccctac	ctgagtccag	60	
ctgtcccctt	ttctgggact	attcaaggag	gtctccagga	cggacttcag	atcactgtca	120	
atgggaccgt	tctcagctcc	agtggaacca	ggtttgctgt	gaactttcag	actggcttca	180	
gtggaaatga	cattgccttc	cacttcaacc	ctcgtttga	agatggaggg	tacgtggtgt	240	
gcaacacgag	gcagaacgga	agctgggggc	ccgaggagag	gaagacacac	atgcctttcc	300	
agaaggggat	gccctttgac	ctctgcttcc	tggtgcagag	ctcagatttc	aagggtgatgg	360	
tgaacgggat	cctcttcgtg	cagtactctc	accgcgtgcc	cttccaccgt	gtggacacca	420	
ttccggtcaa	tggctctgtg	cagctgtcct	acatcagctt	ccagcctccc	ggcgtgtggc	480	
ctgccaaccc	ggctccctatt	accag				506	

```
<210> 189
<211> 399
<212> DNA
<213> Homo sapien
```

<400> 189

ctggacagga	gaagagcctg	jctgctgaag	gcagggctga	cacgaccacg	ggcagcattg	60
ctggagcccc	agaggatgaa	agatcgcaga	gcacagcccc	ccaggcacca	gagtgcctcg	120
accctgcccg	accggctggg	ctcgtgaggc	cgacatctgg	cctttcccag	ggcccaggaa	180

aggaaacctt	ggaaagtgt	ctaategctc	tagactctga	aaaacccaag	aaacttcgt	240
tccacccaaa	gcagctgtac	ttctctgcc	ggcagggtga	gctgcagaag	gtgcttctca	300
tgctgggtga	tgggaattgat	cccaacttca	aaatggagca	ccaaagtaag	cgttcccat	360
tacatgtgtc	tgcggagggt	ggccacgtgg	acatctgcc			399

<210> 190
 <211> 401
 <212> DNA
 <213> Homo sapien

<400> 190						
cggcgacggt	ggtggtgact	gagcggagcc	cggtgacagg	atgttggtgt	tggtattagg	60
agatctgcac	atcccacacc	ggtgcaacag	tttg agct	aaattcaaaa	aactcctggt	120
gccaggaaaa	attcagcaca	ttctctgcac	aggaaaactt	tgacccaaag	agagttatga	180
ctatctcaag	actctggctg	gtgatgttca	tattgtgaga	ggagacttcg	atgagaatct	240
gaattatcca	gaacagaaag	ttgtgactgt	tggacagtcc	aaaattggtc	tgatccatgg	300
acatcaagtt	attccatggg	gagatatggc	cagcttagcc	ctgttgcaga	ggcaatttga	360
tgtggacatt	cttatctcgg	gacacacaca	caaatttgaa	g		401

<210> 191
 <211> 406
 <212> DNA
 <213> Homo sapien

<400> 191						
tggcagccta	agccgtggga	gggttccagt	cgagaatggg	aagatgaaag	acttcagatg	60
gaacagaaat	aatgccttt	tttgacaaac	gcagcagtgc	gtgcctctag	cttgcaagag	120
cgttactccc	cttcatagct	ttaaaagggt	ttgcactgc	gtgcagttag	agtagctaaa	180
tcttgtgtga	cgctccacaa	acacttgtaa	gaattttgca	gagaaagata	accgttgcga	240
cccaatgccc	cccacaggca	ttctactccc	cagtacctct	tagggtggga	gaaatggtga	300
agagttgttc	ctacaacttg	ctaacctagt	ggacagggta	gtagattagc	atcatccgga	360
tagatgtgaa	gaggacggct	gtttggataa	taattaagga	taaaat		406

<210> 192
 <211> 316
 <212> DNA
 <213> Homo sapien

<400> 192						
cccggggagg	ccctggtcat	aaaactttta	attttactag	tgttacttaa	tgtatattct	60
aaaaagagaa	tgcagtaact	aatgccctaa	atgtttgatc	tctgtttgtc	attacttttr	120
caaaattatt	tttttctgta	aagtataata	tataaaactt	cttgcttaaa	ttgaatttct	180
atattagtgg	ttaattgcag	tttattaaag	ggatcattat	cagtaatttc	atagcaactg	240
ttctagtgtt	ttgtgttttt	aaaacagaat	taggaatttg	agatatctga	ttatattttt	300
catatgaatc	acagac					316

<210> 193
 <211> 146
 <212> DNA
 <213> Homo sapien

<400> 193						
gaaacatgga	ctgcccctta	aattttgact	gtcctaaaaa	cctattttctg	atttataata	60
tgctgcctga	taaagtgaca	ctagatgtac	cagctgagtg	tttaactctc	ccatcacaga	120
tcagatttga	gcattaacag	gtattt				146

WO 00/37643

PCT/US99/30909

61

<210> 194
<211> 405
<212> DNA
<213> Homo sapien

<400> 194
cggatgtgct cactgacatt ctactccaag tcggagatgc agatccactc caagtcacac 60
accgagacca agccccacaa gtgcccacat tgctccaaga ccttcgccaa cagctectac 120
ctggcccagc acatccgtat acactcaggg gctaagccct acagttgtaa cttctgtgag 180
aaatccttcc gccagctctc ccaccttcag cagcacaccc gaatccacac tggatgata 240
ccatacaaat gtgcacaccc aggctgtgag aaagccttca cacaactctc caatctgcag 300
tcccacagac ggcaacacaa caaagataaa cccttcaagt gccacaactg tcatcgggcg 360
tacacggatg cagcctcact agaggtgcac ctgtctacgc acaca 405

<210> 195
<211> 421
<212> DNA
<213> Homo sapien

<400> 195
agaattcggc acgagctact ccttgccgcg tcggcactccg cagcctttaa ggttcgcgcg 60
ggggccaggc aagagtttagc catgaagagc ctcaagtcct gcctgaggag gcaggacgtg 120
cccggccccg cgtcgtctgg cgccgcccgc gccagcgcgc atgcagcaga ttggaataaa 180
tatgatgacc gattgatgaa agcagcagaa aggggggatg tagaaaaagt gacgtcaatc 240
cttgctaaaa aggggggtcaa tccaggcaaa ctagatgtgg aaggcagatc tgtcttccat 300
gttggtgacct caaaggggaa tcttgagtggt ttgaatgcc aacctatata tggagttgat 360
attacaacca gtgacactgc agggagaaat gctcttcacc tggctgctaa gtatggacat 420
g 421

<210> 196
<211> 476
<212> DNA
<213> Homo sapien

<400> 196
agaattgata tatagattta atgcaatgcc tactaaaaat ccagtagcat tttttacagg 60
catagacaat agacatagcc aaaacttatt ctaaaaata tatgaagatg cacaggccct 120
agttatacaa tcttgacaaa gaagaataaa gtgggaagaa tctatttgat ttttaaggctt 180
accatgtaac tacagtcac aagagagtgt ggtatcggca gacggtcaga catacagatc 240
aatggaatgt aacagagga ccagaaatag gccacacag atatgctcaa tggatatttg 300
acaagcgtgc aaaacaattc aatggaagaa taagctttca aaaaaatggc gttggagcaa 360
ccggacatcc ataggaaaaa atgaacccat acctaaacca taaaccttat ataaaaataa 420
acacaaaatg aatcataggc ttaaatgtaa gctataaaac ttttagagaa aaacac 476

<210> 197
<211> 503
<212> DNA
<213> Homo sapien

<400> 197
tagccctcgg tgaagcccca gaccacagct atgagtcctc tcgtgtgacg tctgcgcaga 60
aacatgttct gcatgtccag ctcaaccggc ccaacaagag gaatgccatg aacaaggtct 120
tctggagaga gatggtagag tgcttcaaca agatttcgag agacgctgac tgcggggcg 180
tggtgatctc tggtgcagga aaaatgttca ctgcaggtat tgacctgatg gacatggctt 240

PCT/US99/30909

cggacatcct	gcagcccaaa	ggagatgatg	tggcccggat	cagctggtac	ctccgtgaca	300
tcatcactcg	ataccaggag	accttcaacg	tcatcgagag	gtgccccaag	cccggtgattg	360
ctggcctcca	tgggggctgc	attggcggag	gtgtggacct	tgtcacccgc	tgtgacatcc	420
ggtagctgtgc	ccaggatgct	ttcttcagg	tgaaggaggt	ggacgtgggt	ttggctgcc	480
atgtaggaac	actgcagcgc	ctg				503

```
<210> 198
<211> 168
<212> PRT
<213> Homo sapien
```

[illegible]

```
<210> 199
<211> 168
<212> PRT
<213> Homo sapien
```

<400> 199															
His	Arg	Gly	Gly	Gly	Glu	Met	Ala	Phe	Ser	Gly	Ser	Gln	Ala	Pro	Tyr
1				5					10					15	
Leu	Ser	Pro	Ala	Val	Pro	Phe	Ser	Gly	Thr	Ile	Gln	Gly	Gly	Leu	Gln
			20					25					30		
Asp	Gly	Leu	Gln	Ile	Thr	Val	Asn	Gly	Thr	Val	Leu	Ser	Ser	Ser	Gly
		35					40					45			
Thr	Arg	Phe	Ala	Val	Asn	Phe	Gln	Thr	Gly	Phe	Ser	Gly	Asn	Asp	Ile
	50					55					60				
Ala	Phe	His	Phe	Asn	Pro	Arg	Phe	Glu	Asp	Gly	Gly	Tyr	Val	Val	Cys
65					70					75				80	
Asn	Thr	Arg	Gln	Asn	Gly	Ser	Trp	Gly	Pro	Glu	Glu	Arg	Lys	Thr	His
				85					90					95	
Met	Pro	Phe	Gln	Lys	Gly	Met	Pro	Phe	Asp	Leu	Cys	Phe	Leu	Val	Gln
			100					105					110		

WO 00/37643

PCT/US99/30909

63

Ser Ser Asp Phe Lys Val Met Val Asn Gly Ile Leu Phe Val Gln Tyr
 115 120 125
 Phe His Arg Val Pro Phe His Arg Val Asp Thr Ile Ser Val Asn Gly
 130 135 140
 Ser Val Gln Leu Ser Tyr Ile Ser Phe Gln Pro Pro Gly Val Trp Pro
 145 150 155 160
 Ala Asn Pro Ala Pro Ile Thr Gln
 165

<210> 200
 <211> 132
 <212> PRT
 <213> Homo sapien

<400> 200
 Gly Gln Glu Lys Ser Leu Ala Ala Glu Gly Arg Ala Asp Thr Thr Thr
 1 5 10 15
 Gly Ser Ile Ala Gly Ala Pro Glu Arg Glu Arg Ser Gln Ser Thr Ala
 20 25 30
 Pro Gln Ala Pro Glu Cys Phe Asp Pro Ala Gly Pro Ala Gly Leu Val
 35 40 45
 Arg Pro Thr Ser Gly Leu Ser Gln Gly Pro Gly Lys Glu Thr Leu Glu
 50 55 60
 Ser Ala Leu Ile Ala Leu Asp Ser Glu Lys Pro Lys Lys Leu Arg Phe
 65 70 75 80
 His Pro Lys Gln Leu Tyr Phe Ser Ala Arg Gln Gly Glu Leu Gln Lys
 85 90 95
 Val Leu Leu Met Leu Val Asp Gly Ile Asp Pro Asn Phe Lys Met Glu
 100 105 110
 His Gln Ser Lys Arg Ser Pro Leu His Ala Ala Ala Glu Ala Gly His
 115 120 125
 Val Asp Ile Cys
 130

<210> 201
 <211> 120
 <212> PRT
 <213> Homo sapien

<400> 201
 Met Leu Val Leu Val Leu Gly Asp Leu His Ile Pro His Arg Cys Asn
 1 5 10 15
 Ser Leu Pro Ala Lys Phe Lys Lys Leu Leu Val Pro Gly Lys Ile Gln
 20 25 30
 His Ile Leu Cys Thr Gly Asn Leu Cys Thr Lys Glu Ser Tyr Asp Tyr
 35 40 45
 Leu Lys Thr Leu Ala Gly Asp Val His Ile Val Arg Gly Asp Phe Asp
 50 55 60
 Glu Asn Leu Asn Tyr Pro Glu Gln Lys Val Val Thr Val Gly Gln Phe
 65 70 75 80
 Lys Ile Gly Leu Ile His Gly His Gln Val Ile Pro Trp Gly Asp Met
 85 90 95
 Ala Ser Leu Ala Leu Leu Gln Arg Gln Phe Asp Val Asp Ile Leu Ile
 100 105 110
 Ser Gly His Thr His Lys Phe Glu

WO 00/37643

PCT/US99/30909

64

115

120

<210> 202
<211> 135
<212> PRT
<213> Homo sapien

<400> 202
Arg Met Cys Ser Leu Thr Phe Tyr Ser Lys Ser Glu Met Gln Ile His
1 5 10 15
Ser Lys Ser His Thr Glu Thr Lys Pro His Lys Cys Pro His Cys Ser
20 25 30
Lys Thr Phe Ala Asn Ser Ser Tyr Leu Ala Gln His Ile Arg Ile His
35 40 45
Ser Gly Ala Lys Pro Tyr Ser Cys Asn Phe Cys Glu Lys Ser Phe Arg
50 55 60
Gln Leu Ser His Leu Gln Gln His Thr Arg Ile His Thr Gly Asp Arg
65 70 75 80
Pro Tyr Lys Cys Ala His Pro Gly Cys Glu Lys Ala Phe Thr Gln Leu
85 90 95
Ser Asn Leu Gln Ser His Arg Arg Gln His Asn Lys Asp Lys Pro Phe
100 105 110
Lys Cys His Asn Cys His Arg Ala Tyr Thr Asp Ala Ala Ser Leu Glu
115 120 125
Val His Leu Ser Thr His Thr
130 135

<210> 203
<211> 135
<212> PRT
<213> Homo sapien

<400> 203
Leu Leu Leu Ala Arg Trp His Ser Ala Ala Phe Lys Val Arg Ala Gly
1 5 10 15
Ala Arg Gln Glu Leu Ala Met Lys Ser Leu Lys Ser Arg Leu Arg Arg
20 25 30
Gln Asp Val Pro Gly Pro Ala Ser Ser Gly Ala Ala Ala Ser Ala
35 40 45
His Ala Ala Asp Trp Asn Lys Tyr Asp Asp Arg Leu Met Lys Ala Ala
50 55 60
Glu Arg Gly Asp Val Glu Lys Val Thr Ser Ile Leu Ala Lys Lys Gly
65 70 75 80
Val Asn Pro Gly Lys Leu Asp Val Glu Gly Arg Ser Val Phe His Val
85 90 95
Val Thr Ser Lys Gly Asn Leu Glu Cys Leu Asn Ala Ile Leu Ile His
100 105 110
Gly Val Asp Ile Thr Thr Ser Asp Thr Ala Gly Arg Asn Ala Leu His
115 120 125
Leu Ala Ala Lys Tyr Gly His
130 135

<210> 204
<211> 167
<212> PRT

WO 00/37643

PCT/US99/30909

65

<213> Homo sapien

<400> 204

```

Ala Leu Gly Glu Ala Pro Asp His Ser 10 Glu Ser Leu Arg Val Thr
 1          5          10          15
Ser Ala Gln Lys His Val Leu His Val Gln Leu Asn Arg Pro Asn Lys
          20          25          30
Arg Asn Ala Met Asn Lys Val Phe Trp Arg Glu Met Val Glu Cys Phe
          35          40          45
Asn Lys Ile Ser Arg Asp Ala Asp Cys Arg Ala Val Val Ile Ser Gly
          50          55          60
Ala Gly Lys Met Phe Thr Ala Gly Ile Asp Leu Met Asp Met Ala Ser
65          70          75          80
Asp Ile Leu Gln Pro Lys Gly Asp Asp Val Ala Arg Ile Ser Trp Tyr
          85          90          95
Leu Arg Asp Ile Ile Thr Arg Tyr Gln Glu Thr Phe Asn Val Ile Glu
          100          105          110
Arg Cys Pro Lys Pro Val Ile Ala Ala Val His Gly Gly Cys Ile Gly
          115          120          125
Gly Gly Val Asp Leu Val Thr Ala Cys Asp Ile Arg Tyr Cys Ala Gln
          130          135          140
Asp Ala Phe Phe Gln Val Lys Glu Val Asp Val Gly Leu Ala Ala His
145          150          155          160
Val Gly Thr Leu Gln Arg Leu
          165

```

<210> 205

<211> 381

<212> DNA

<213> Homo sapien

<400> 205

```

aaatttggga tcatgcctg ttctgaaaac tagatgcacc aaccgtatca ttatttgttt      60
gaggaaaaaa agaaatctgc attttaattc atgttggtca aagtcgaatt actatctatt      120
tatcttatat cgtagatctg ataacctat ctaaaagaaa gtcacacgct aaatgtattc      180
ttacatagtg cttgtatcgt tgcatttggt ttaatttggt gaaaagtatt gtatctaact      240
tgtattactt tggtagtttc atctttatgt attattgata tttgtaattt tctcaactat      300
aacaatgtag ttacgctaca acttgcttaa aacattcaaa cttgttttct tttttctggt      360
gttttctttg ttaattcatt t
                                     381

```

<210> 206

<211> 514

<212> DNA

<213> Homo sapien

<400> 206

```

aaaagtaaat tgcataaaat tacatccaat ttctttctct aaaccaacat attcttcacc      60
ttcacaaagc aaacacatgg tgcactgaaa ccgagggtgt accagcttta catactgttc      120
tgccatttgt ggggggtgca accacaacat aagtcagaaa aaaagctatc cagcttttcg      180
tggaatctgg tgaagtttac acttagcgat aagcctctaa gcctgaactt agcagggcta      240
gcaaaacttt atttatttcc taactcctat tatttttagaa tggttttcaa aataatactg      300
caagttccta attgaaatac aaaacagaac aaaaagctgt gagaaatctt ttttttctt      360
tggctcctta aagacttggg ataatttata ttagtggtgc atacatttta cttctacat      420
ttgatgtac ttgctcttga aagcactaga acaaattaat tgaaataaaa cctctctgaa      480
accatttgaa tctttgatcc taccatagag tttt
                                     514

```

WO 00/37643

PCT/US99/30909

66

<210> 207
 <211> 522
 <212> DNA
 <213> Homo sapien

 <220>
 <221> misc_feature
 <222> (1)...(522)
 <223> n = A,T,C or G

<400> 207
 caagcttttg gtgcatagca gccngcctgg aagcatt gg agtgctctgt ctgccctggt 60
 ggggtttcatt atcctgtctg tcaaacaggc caccttaaatt cctgcctcac tgcagtgtga 120
 gttggacaaa aataatatac caacaagaag ttatgtttct tacttttatac atgattcact 180
 ttataccacg gactgctata cagccaaagc cagtctggct ggaactctct ctctgatgct 240
 gatttgcaact ctgctggaat tctgcctagc tgtgctcact gctgtgctgc ggtggaaaca 300
 ggcttactct gacttccctg ggagtgtact ttctctgct cacagttaca ttggtaattc 360
 tggcatgtcc tcaaaaatga ctcatgactg tggatatgaa gaactattga cttcttaaga 420
 aaaaaggag aaataatgaat cagaaagttg attcttatga taatatggaa aagttaacca 480
 ttatagaaaa gcaaagcttg agtttcttaa atgtaagctt tt 522

<210> 208
 <211> 278
 <212> DNA
 <213> Homo sapien

<400> 208
 aaaaagcact accccttttt tccaacacgg agcttaaaac aaattaatga aagagtggaa 60
 aattcaaaat aagggraaga gataagggtt tttttttttt tcctttaaga tagactcagg 120
 ataggtagat agctttcact gatgtagatg tggataaat tactactca ggaaaaaaat 180
 tcccaaacat cttatgaaaa agtatacaac tctacttcaa aatatgctat ttactcactg 240
 ccaaagacag ttttatttga aatcttgtt ctgtattt 278

<210> 209
 <211> 234
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc feature
 <222> (1)...(234)
 <223> n = A,T,C or G

<400> 209
 cctcccaaatt ttagcagggtg ctgggnagga ccctagggag tggtttatgg gggctagctg 60
 gtgaaactgc cctttccttt ctgttctatg agtgtgatgg tgtttgagaa aatgtggggc 120
 tatggttcag gcgcacttca catgtgcaaa gatggagaaa gcactcacct acacgtttag 180
 gctcagaatg ttgattgaaa cattttgaat gatcaaaaat aaaatggtat tttt 234

<210> 210
 <211> 186
 <212> DNA
 <213> Homo sapien

WO 00/37643

PCT/US99/30909

67

<220>

<221> misc_feature

<222> (1)...(186)

<223> n = A,T,C or G

<400> 210

```

aaaataactg atggcaaaat aaaanattta catcacatca tactgtgtaa acatgtaagg      60
tctctgtaca aagaaatata catgcaaaat aatgtaaaaa ttttaactgaa ataataaaaag    120
aaacaatata caaataaaaa ttatgaggtt acgaatacac atccagtttc gaatccaatt      180
tctttt                                           186

```

<210> 211

<211> 403

<212> DNA

<213> Homo sapien

<400> 211

```

aaaaattggt aaaatattta agtacaaaat aagtagcttc cagcgagggt tttataccat      60
agtaagagca cacaatagat attactagca cacatgggtt atctgggagc gctatagcta    120
caataaacct aattatggaa cagaaatttg cattctgttt ccagtgtctac tacactccta    180
ctttctcaaa agtctgtctt attaatatca gctcagtgcg gtttactatg aatagtttat    240
gtctgtgatg caaagcatta attgttctct ttttacaac atacattttt ttcataagga    300
agactggggg aaaacccaga aacatacaga gaaaaggaaa gcatcatcaa atatatgtta    360
aaaattaaga tgatgtttac tactagtcac cctacaacaa ttt                                           403

```

<210> 212

<211> 345

<212> DNA

<213> Homo sapien

<400> 212

```

cctctttatg agttcattac tgctgttcag tctcggcaca cagacacccc tgtgcaccgg      60
ggtgtacttt ctactctgat cgctgggcct gtggttgaga taagtcacca gctacggaag    120
gtttctgacg tagaagagct taccctccca gagcatcttt ctgatcttcc accattttca    180
aggtgtttta taggaataat aataaagtct tcgaatgtgg tcaggtcatt tttggatgaa    240
ttaaaggcat gtgtggcttc taatgatatt gaaggcattg tgtgcctcac ggctgctgtg    300
catattatcc tggttattaa tgcaggtaaa cataaaagct caaaa                                           345

```

<210> 213

<211> 318

<212> DNA

<213> Homo sapien

<400> 213

```

aaaatgtttt attattttga aaataatggt gtaattcatg ccagggactg acaaaaagact      60
tgagacagga tggttattct tgtcagctaa ggtcacattg tgcttttttg accttttctt    120
cctggactat tgaaatcaag cttattggat taagtgatat ttctatagcg attgaaaggg    180
caatagttaa agtaatgagc atgatgagag tttctgttaa tcatgtatta aaactgattt    240
ttagctttac aaatatgtca gtttgcagtt atgcagaatc caaagtaaat gtccctgctag    300
ctagttaagg attgtttt                                           318

```

<210> 214

<211> 462

<212> DNA

<213> Homo sapien

WO 00/37643

PCT/US99/30909

68

<400> 214

aaacacatct	ggttctggca	gcaagttata	ttatgcattt	agagcaatag	gtgccctgaa	60
agttattgtt	gctttttttg	tttttttttt	cagtttgtgc	gtgtcacttg	aatcagaaac	120
caaacacatg	taaaaaaata	tcatectcaa	tgccccccat	taactctctc	tccagaaggt	180
gacaatgtta	gtgaactcaa	gactctcact	gatgatggta	ttttacaatg	aaaacacaag	240
gaaacccttt	gagggtccaat	tttcacatca	tattctccaa	atagtaaaat	agcagctcta	300
catgttgatg	aaaagaaatt	tcaattttct	cctatttgtt	tttactcata	tcaacattaa	360
tatgtatctg	gatttattaa	tttccaaaaa	gaaaatttta	gttaccaaat	atttcagaaa	420
tttaataaag	cattatatat	atgtaattag	cacttatcta	cc		462

<210> 215

<211> 280

<212> DNA

<213> Homo sapien

<400> 215

aaacttttct	gaaacgatta	gctgtagcca	aattatgtgg	ttacgttttg	ctacattaga	60
atttgaaaat	gcaatatgtg	tggtaaatct	actgtttgaa	atttataatg	gtctctgata	120
tgattcgaat	tttggttaact	tttgaaagtt	atcttcccc	tttagtcatg	gatttctatt	180
tgttttttta	tgtaattttt	tctagaaagc	atctgaattg	actaggcttt	tcctatataa	240
aaaactcaaa	acttggttaac	tctgtacttt	aataaaattt			280

<210> 216

<211> 210

<212> DNA

<213> Homo sapien

<400> 216

aaaatctctg	gcttcaaagt	ttcttgggga	aaggctcggt	tacctcacat	tttttgtttc	60
cattagtaat	attctaggta	cctcacaaaa	tgtattatgg	tgccatggct	gttagttttt	120
agtgagtgtc	gtaggattaa	ttcgaaaata	ggcagaattc	cattcctccc	aagggtggcaa	180
aaattagcta	tactgargta	attgtcattt				210

<210> 217

<211> 398

<212> DNA

<213> Homo sapien

<400> 217

ctggagctgc	tagaacttga	gatgagggca	agaacgatta	aagccctaata	gaaagctggg	60
gatataaaaa	agccagccta	ggtattttaac	ttgattttga	atttttaggta	tgtttgaaca	120
aagccacatc	atttaatttt	gtatctaaaa	tttatttggg	gtcttatatg	ttattttctca	180
tgtaaccttt	attaggactc	attttagccc	taaattacct	gtggctgttt	ctttttattt	240
ttttgactac	ttttatatta	taaatgtgtg	ttactgtctt	atgaattcat	ggcaatatag	300
ttggatagcc	tggtactttt	gttagatgag	tatttagctg	tgtctgcaaa	tcttaaaagc	360
cattagcaaa	gagtcgtggg	atttttttct	ttattttt			398

<210> 218

<211> 487

<212> DNA

<213> Homo sapien

<400> 218

ctgccgccgg	tcaggctggg	taaagatcag	gtcccccagg	accttgcgat	ttatgtcgcc	60
------------	------------	------------	------------	------------	------------	----

WO 00/37643

PCT/US99/30909

69

```
attctccagc aagacctcag tgccgaagac ctctacgatg cgccggtggg cagggatcc 120
tggtgcacg acgtgccggg ccatcacgtc cacgtcaatc accgcacagc ccagtttcag 180
tgtttttaca cattatattg ttataatctc acaataacta taaattaggt agaacaggaa 240
atgaggtttg gagaagatac ttgacttata cgaccatctg tacttggtccc atagtaagga 300
gcctcaagca gagacaaagg aggaagtgtc ctatgttgta tggtttacag gccataaatg 360
aatgtcatct ttttctctcc ctggggaaaa atgtctcaaa aatcccacca taggacatga 420
catctccaga acctctatta caaaatacac atttctgtga gaggggtaac aaatttggtg 480
taacctg 487
```

<210> 219

<211> 390

<212> DNA

<213> Homo sapien

<400> 219

```
aaaaaataca ccacacgata caactcaata caggagtatt ttttctcaaa ttttcttagc 50
accatcaaca ttcttcaagt atctgaaata ctattaatta gcacctttgt attatgaaca 120
aaacaaaaca aggacctcag ttcattctctg tctaggtcag cacctaacaa tgtggatcac 180
actcatggga aagtgttttg aggtagttta aacctttgga agtttgggtt ttaacttcc 240
ctctgtggaa gatattcaaa agccacaagt ggtgcaaatg tttatggtt ttatttttca 300
atttttattt tggttttctt acaaagggtg acattttcca taacaggtgt aagagtgttg 360
aaaaaaaagt tcaaattttt gggggagcgg 390
```

<210> 220

<211> 341

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(341)

<223> n = A,T,C or G

<400> 220

```
aaaacaggca aagttttaca gagaggatac atttaataaa actgcgagga catcaaagtg 60
gtaaatactg tgaaatacct tttctnnnca aaaggcaaat attgaagttg tttatcaact 120
tcgctagaaa aaaaaaaca cttggcatac aaaatattta agtgaaggag aagtctaacg 180
ctgaactnnn aatgaaggga aattgtttat gtgttatgaa catccaagtc tttcttcttt 240
tttaagttgt caaagaagct tccacaaaat tagaaaggac aacagttctg agctgtaatt 300
tcgccttaaa ctctggacac tctatatgta gtgcattttt a 341
```

<210> 221

<211> 234

<212> DNA

<213> Homo sapien

<400> 221

```
ccagggggaa ttgaggagg ctctaagcta ggggcactgc atggtgggac aggatggccc 60
cttgaggact gaaccttggg gagaagacaa acagtaataa taaaaacaaa taacaagtac 120
tttaagaatg gattgtatga cctatagtga cagatgacat cactaatact gaaagcttct 180
tatattaata attttggtcaa aatgtcattt tgtaatatag tatatgcttt ccag 234
```

<210> 222

<211> 186

<212> DNA

WO 00/37643

PCT/US99/30909

70

<213> Homo sapien

<400> 222

aaattttcat	tgagttgtcc	atctccagca	tatagggctt	caggagcaga	gcagaccttg	60
tttttagtgg	ttccatggga	taaaatggga	ttggaggagc	tagaagaatt	cagggctctgg	120
tccaatctgc	cagtcttctc	gaaatatcga	aaatacacca	gggctgctat	atcagagcca	180
ccctgg						186

<210> 223

<211> 486

<212> DNA

<213> Homo sapien

<400> 223

ccataagcag	ataagtagca	gttcaactgg	atgtctctct	tctccaaatg	ctacagtaca	60
aagccctaag	catgagtggg	aaatcggtgc	ttcagaaaag	acttcaaata	acacttactt	120
gtgcttggtc	gtgctggatg	gtatattctg	tgtcattttt	cttcattggg	gaaacagccc	180
acagagctca	ccaacaagta	ctccaaaact	aagtaagagt	ttaagctttg	agatgcaaca	240
agatgagcta	atcgaaaagc	ccatgtctcc	tatgcagtac	gcacgatctg	gtctgggaac	300
agcagagatg	aatggcaaac	tcatagctgc	aggtggctat	aacagagagg	aatgtcttcg	360
aacagtcgaa	tgtctataat	cacatacaga	tactgggtcc	tttctctgct	ccatgagaac	420
accaagagcc	cgatttcaaa	tggtgtact	catgggccag	ctctatgtgg	taggtggatc	480
aaatgg						486

<210> 224

<211> 322

<212> DNA

<213> Homo sapien

<400> 224

aaatgttcac	tatgtcattt	agtgtccaac	tttacggata	ggttgactat	ctaaataggc	60
attttttagtc	attaaaaaaa	aatctagtca	ccaggaggat	ccctataact	caaaaataact	120
tgtttgtaaa	agaaaatttg	tttacttacc	cattagtaag	ttcctgcata	ttcattataa	180
gatggcaaat	caaaactttt	taggatgaag	acagcttatt	tttaagtgtg	atagtcttag	240
ttgggttagg	gtctcaattt	taattaataa	aatacttggg	ttttatttgc	ttgtcctttt	300
gaattcctgt	tttaataatt	tt				322

<210> 225

<211> 489

<212> DNA

<213> Homo sapien

<400> 225

aaatgtagga	ataaaatggc	tggcatctaa	gcactttagt	aaaagagggt	tttacaaata	60
actaaggatt	gtagagcttc	cttctctttt	ttttcttttt	tctttctttt	gttttacatg	120
aactcaactt	attcctaaca	tttgtctacc	tcaaagaaat	ttcaagatta	tttagataac	180
atggatatgt	gccaaatcct	ttgagctggt	aagatgataa	tttctgctt	tcctcctaca	240
tcttctctct	ccactccctc	ctttgggtgtg	aatattggct	tccaatttaa	gacctttttt	300
ttttttttcc	agtttggttt	agcttattat	aggttttgga	ggaactttgc	cattttgtaa	360
tctttcaaat	cattcttcac	ccttcctcac	atcagcttcc	tgcttttccc	agtgttttac	420
tgtaaatgtg	gtagcatatg	acaaatcttg	agctgacttt	cctcttcact	gatgtcatct	480
tgagctctt						489

<210> 226

<211> 398

WO 00/37643

PCT/US99/30909

71

<212> DNA

<213> Homo sapien

<400> 226

```

caagggccca cgcagagca cacctatgct atggggagcc ctgctggcag ccccgagagc      60
catgccatgg cctgcaggag ccaggctcct gtgtggatga agtcctctct cctctgtgcc      120
ttgatccctt gggggtgctt ttggtcatct cttctgtcct ttctgtctc tgaaatagtc      180
atcactcccc ttgactctct ctgttcacgt cttctcagtc tgcagagtta acttctgtaa      240
ggagtttaat ctgggggttc aagaaaacaa gtcccttggt aacatagcac tgactttgca      300
acaatagaaa actaacaat gagcaacaat ataaagagta gaggtagttc tcattgggtg      360
taacttcaac ccattctgct tgtggttaga atttataa      398

```

<210> 227

<211> 535

<212> DNA

<213> Homo sapien

<400> 227

```

ctgctgcata gaaaatatgc taacatacaa cagtcaagtt taagcctgtg catagagaag      60
ataaaagcact tatggtaact gcaaatggta acgagtcctt aaggtttgta caacctagta      120
tgggtccata aggaaaaact gtagtagaaa tgggttaggac aaacaataaa gtagaaacag      180
gggggaaact tgagaagaga agaaagaagc aagaaaaaaa gactttcaat tgtataaaat      240
tcacaaacca gtaaagtata aagacaccat ggagaaatgg ttaactctgc cccaaacacc      300
caacagcaaa caaaaccaga atgaataagc ctttggcaga caattttaga aatttgaatg      360
ttacatttct caataattca caaacaatat attatatggt atatttatat taaatattgg      420
gaaaccaatg ttgtaaattt gatgcttata atgcttttagc caatgagagc acaatgatat      480
caatcaagct aaatgaatgc tgggtgtatc acaacagtcg tcatttatga aacaa      535

```

<210> 228

<211> 301

<212> DNA

<213> Homo sapien

<400> 228

```

aaacaataaa caccatcaac cttattgact ttattgtccc ttaaattata ttgactgttg      60
tgattccatc aagtittgtac actcttttct ctccctgttt tgcagcaaca aattgcgaag      120
tgcttttggt tgtttgtttt cgtttggtta aagcttattg ccatgctggt gcggtatgg      180
agactgtctg gaaggcttgg aatggtttat tgcttatggt aaaatttgcc tgatttctta      240
caggcagcgt ttggaacctt tttattatat agttgtttac atacttataa gtctatcatt      300
t

```

<210> 229

<211> 420

<212> DNA

<213> Homo sapien

<400> 229

```

aaagttgctt tgctggaagt ttttataagg aatctcagat taaaccttta gaagtttaat      60
tgacactagg aagccaaacc aaggctgact tcagactttg tttgtagtac ctgtgggttt      120
attacctatg ggtttatata ctcaaatacg acattctagt caaagtcttg gtaatataac      180
caatgttttc aaatgtattc tgcatacaa agagcagatt tttattgaac ttgtgcaata      240
actatattac catacaatat aaatattcat gaatagtttc ccaagtctgg agcgaccaca      300
tagggagaaa atgcaaatgt ctcaattttt gttcacaaaa gtatatttta tcaaattgct      360
gtaagctgtg gatagcttaa aagaaaaaaa gtttcctgaa atctgggaaa caagacattt      420

```

WO 00/37643

PCT/US99/30909

72

<210> 230
<211> 419
<212> DNA
<213> Homo sapien

<400> 230
gtgaagtcct aaagcttgca ttccaccagc ttctacaata gccggcttat tactagagca 60
gacagatagc accttcagca ctctgcttgt ggtccacagt agtttttcgt aagtataggt 120
cctcattata ttactaaaag cttgggggtcc accactagcc agtatgatga gcttgctttc 180
ttggttgcca taagctaaaa ttggaaggca gtctgtcgta atagccaaga atttaacatt 240
tgttttgttg agcaaggcaa ccattttctg cagcccacca gctaaacgca ctgccatttt 300
agctccttct tgatgtaata aaaggttgtg gagagttgta atggcataaa acaacacaga 360
atccactggc taaccaagca ttttcaccag ggcaggaatg cctccagact taaagatgg 419

<210> 231
<211> 389
<212> DNA
<213> Homo sapien

<400> 231
ttgttcagag ccctggtgga tcttgcaatc cagtgcctta caaaggctag aacactacag 60
gggatgaatt cttcaaatag gagccgatgg atctgtggtc ctttgggact catcaaagcc 120
ttggtttagc attttgtcag ttttatcttc agaaattctc tgcgattaag aagataattt 180
attaaaggtg gtccttccta cctctgtggt gtgtgtcgcg cacacagctt agaagtgcta 240
taaaaaagga aagagctcca aattgaatca cctttataat ttaccattt ctatacaaca 300
ggcagtggaa gcagtttcag agaacttttt gcattgcttat ggttgatcag ttaaaaaaga 360
atgttacagt aacaaataaa gtgcagttt 399

<210> 232
<211> 397
<212> DNA
<213> Homo sapien

<400> 232
ccaggataat atacacaggt ttgcagctaa aactgtgcac agtgggtcat tgatgctagt 60
cacagtggaa ctgaaggaag gctctacagc ccagcttacc ataaacactg agaaaactgt 120
gattggctct gttctgtctg gggaactgaa gctgtgctcg tctcaggggt aacctgctta 180
catctggact ttagaatctg gcacacaaca aaagtgcctg gcattccacta ctgctgcctt 240
tcatttataa taatagccct tccatctggc agtgggggaa gaatacactc ttgacattct 300
tgtctcctgc tttagaatgc tagtgtgtat ctatcatgta tgcaataactt tccccctttt 360
tgctttgcta accaaagagc atatatttta ctgtcag 397

<210> 233
<211> 508
<212> DNA
<213> Homo sapien

<400> 233
cgaggagtgc cttaagtgcg aggacctcaa agtgggacaa tatatttgta aagatccaaa 60
aataaatgac gctacgcaag aaccagttaa ctgtacaaac tacacagctc atgtttcctg 120
ttttccagca cccaacataa cttgtaagga ttccagtggc aatgaaacac attttactgg 180
gaacgaagtt ggttttttca agcccatatc ttgccgaaat gtaaatggct attcctacaa 240
agtggcagtc gcattgtctc tttttcttgg atggttggga gcagatcgat ttacacctgg 300
atacctgct ttgggtttgt taaagttttg cactgtaggg ttttgtggaa ttgggagcct 360
aattgatttc attcttattt caatgcagat tgttggacct tcagatggaa gtagttacat 420

WO 00/37643

PCT/US99/30909

73

tatagattac tatggaacca gacttacaag actgagtatt actaatgaaa catttagaaa 480
aacgcaatta tatccataaa tattttttt 508

<210> 234

<211> 358

<212> DNA

<213> Homo sapien

<400> 234

aaatgttggt attcaaaacc aaagatataa ccgaaaggaa aaacagatga gacataaaat 60
gatttgcaag atgggaaata tagtagttta tgaatgtaaa tttaaattcca gttataatag 120
tgyctacaca ctctcactac acacacagac cccacagtc tatatgccac aaacacattt 180
ccataaacttg aaaatgagta ttttgcatat ctcagttcag gatatgtttt ttacaagtta 240
atcctaaagt cataaagcaa gaagctattc atagtacaag attttatttg ctaagcttta 300
caaattaaac tctaaaaaat tattacaatg atactgaaag atattttatt ggcctttt 358

<210> 235

<211> 482

<212> DNA

<213> Homo sapien

<400> 235

gaagaaagtt agatttacgc cgatgaatat gatagtgaat tggatttttg cgtaggtttg 60
gtctagggtg tagcctgaga ataggggaaa tcagtgaatg aagcctccta tgatggcaaa 120
tacagctcct attgatagga catagtggaa gtgagctaca acgtagtacg tgtcgtgtag 180
tacgatgtct agtgatgagt ttgctaatac aatgccagtc aggccacctt cggtgaaaag 240
aaagatgaat cctagggctc agagcactgc agcagatcat ttcataltgc ttccgtggag 300
tgtggcgagt cagctaaata ctttgacgcc ggtggggata gcgatgatta tggtagcgga 360
ggtgaaatat gctcgtgtgt ctacgtctat tctactgta aatatatggt gtgctcacac 420
gataaaccct aggaagccaa ttgatatcat agctcagacc atacctatgt atccaaatgg 480
tt 482

<210> 236

<211> 149

<212> DNA

<213> Homo sapien

<400> 236

cctcttcatt gttcacatgt cacaggagga ggctctgagc aaaggccact ggcaagttag 60
ggcaacacca agaaggctct gcggagagac tccctgtggg ttggggcctg gcaggaacgg 120
tgccctgtgga ctgtttatgg tctgtccag 149

<210> 237

<211> 391

<212> DNA

<213> Homo sapien

<400> 237

gaagctaaat ccaaagaaat atgaaggtgg ccgtgaatta agtgatttta ttagctatct 60
acaagagaa gctacaaacc cccctgtaat tcaagaagaa aaacccaaga agaagaagaa 120
ggcacaggag gatctctaaa gcagttagcca aacaccactt tgtaaaaagga ctcttccatc 180
agagatggga aaaccatttg ggaggactag gacccatatt ggaattatta cctctcaggg 240
ccgagaggac agaattggata taatctgaat cctgtttaaatt tttctctaaa ctgtttctta 300
gctgcactgt ttatggaaat accaggacca gtttatgttt gtgggttttg gaaaaattat 360
ttgtgttggg ggaaatgttg tgggggtggg g 391

<210> 238
<211> 374
<212> DNA
<213> Homo sapien

<400> 238
aaaaaacaaa acaatgtaag taaaggatat ttctgaatct taaaattcat cccatgtgtg 60
atcataaact cataaaaaata attttaagat gccggaaaag gatactttga ttaaataaaa 120
acactcatgg atatgtaaaa actgtcaaga ttaaaattta atagtttcat ttatttgta 180
ttttatttgg aagaaatagt gatgaacaaa gacccctttt catactgata cctgggtgta 240
tattatttgg tgcaacagtt ttctgaaatg atatttcaaa ttgcatcaag aaattaaaat 300
catctatctg agtagtcaa atacaagtaa aggagagcaa ataaacaaca tttggaaaaa 360
aaaaaaaaaa aaaa 374

<210> 239
<211> 200
<212> DNA
<213> Homo sapien

<400> 239
aaagatgtct ttgaccgcat atgtactgga aatttcaaac gtggatcttc ccaggttgta 60
gtctttgtgt tatgatcaat gaagaagggc cggccgtttg gcgctatcct catttcccag 120
ccgggtggca agaagctctg tgtgactttg tgttgtgggt tgggggaggt gtaaggtgat 180
ggctgtgggg actgtgggtt 200

<210> 240
<211> 314
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (314)
<223> n = A,T,C or G

<400> 240
ctggtaaaact gtccaaaaca aggttccaaa taacacctct tactgattta ccctacccat 60
acatatncca natagntttt gatcaaaaac atgaaatana tccacctgct tattttaage 120
atattaaaaa ggaaactaat tggaccattt tctatttgct tattttatac aaaaaggcta 180
cacaattgat acactctatt cagataacaa tcaattagag tgantatgaa ttactggcga 240
caccatcact caattcttaa aaattagaaa ttgctgtagc agtattcact ataacttaac 300
actaccgaga gact 314

<210> 241
<211> 375
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (375)
<223> n = A,T,C or G

<400> 241

PCT/US99/30909

ccaagtcctt	ggagttatag	gatattcatt	acttcctctc	attgtaatag	ccctgtact	60
tttggtggtt	ggatcatttg	aagtgggtgc	tacacttata	aaactgtttg	gtgtgttttg	120
ggctgcctac	agtgtctgct	cattgttagt	gggtgaagaa	ttcaagacca	aaaagcctct	180
tctgatttat	ccaatctttt	tattatacat	ttatcttttg	tcggtatata	ctggtgtgtg	240
atccaagtta	tacatgaata	gaaaaagatg	gtgttaaatt	tgtgtgtagg	ctgggaattc	300
tngctaaagg	aatggnaaaa	aacctgtntt	tgnaaaattt	acntgtccca	aagnnaagga	360
anctaaacgc	ttttt					375

```
<210> 242
<211> 387
<212> DNA
<213> Homo sapien
```

<400> 242									
aaaggcattc	tctgatttac	atgagaattg	agaaactgag	atgtatgatt	tgtctgttag				60
tcaatttcac	accctttcat	tctcataagc	cccaaatttt	gctcagttaa	ggagcttgct				120
ttaggcccac	ctatgtaagt	ctgttatact	agctaattgtg	cccatttgaa	tagttcaagg				180
gtcagctaatt	gctctgagct	tcattggctcc	agtataaaga	acaaatttaa	caaaattaag				240
ctgttactgt	agccgagtta	cccttctgct	ccacacatat	gtagtgggat	cttcaggat				300
ttccatagtg	ccaattatca	aaggccttga	ctacttagca	ttgctgtatt	acagatgtgc				360
aaactgaggc	actgaaaagt	caaatttt							387

```
<210> 243
<211> 536
<212> DNA
<213> Hcmo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(536)
<223> n = A,T,C or G
```

<400> 243							
aaacccaaaag	gacgaagaaa	aaacactttn	aaaaaaaaaa	aaaaaaaaaga	aaaacccaac		60
catatttttgc	cacatgtgag	agtacggtca	agcagtattt	acaaaaagggt	taacggaaca		120
acactctgac	acatgctctg	agaatactgg	gactgctgtt	tcaaaaaaaa	aggttcaaac		180
ttattgtcac	agcatcatca	caaaatagag	gatcaccatt	ggtttgcttg	gcttttcttt		240
tttttttttc	cccaagtgag	gacctaaactc	caaataatac	aatagaatat	gcaaattatc		300
ttcacatcaa	gagtacccca	agaaaaacga	aatccatggc	acanacactg	tacaagggtg		360
cagggcaggg	ctctgagggg	cccaaaccctc	attttgccaa	ctcgattttc	tagcattgaa		420
ggggagcaagg	ggtcaggcat	atgatggaga	tgatactgaa	atgattttatc	caaaatccat		480
gcaaatacaag	ttctttggat	agaggtgaan	aacttggaaca	tggctgtttc	aggcag		536

```
<210> 244
<211> 397
<212> DNA
<213> Homo sapien
```

<400> 244						
ccaggataat	atacacaggt	ttgcagctaa	aactgtgcac	agtgggtcat	tgatgctagt	60
cacagtggaa	ctgaaggaag	gctctacagc	ccagcttatac	ataaacactg	agaaaactgt	120
gattggctct	gttctgctgc	gggaactgaa	gcctgtcctg	tctcaggggt	aacctgctta	180
catctggact	ttagaatctg	gcacacaaca	aaagtgcctg	gcataccta	ctgctgcctt	240
tcatttataa	taatagccct	lccatctggc	agtgggggaa	gaatacactc	tgtgacattct	300
tgtctcctgc	tttagaatgc	tagtgtgtat	ctatcatgta	tgcaataactt	tccccctttt	360

tgctttgcta accaaagagc atatatttta ctgtcag 397

<210> 245
<211> 508
<212> DNA
<213> Homo sapien

<400> 245
cgaggagtgc cttaagtgcg aggacctcaa agtgggacaa tatatttgta aagatccaaa 60
aataaatgac gctacgcaag aaccagttaa ctgtacaaac tacacagctc atgtttcctg 120
ttttccagca cccaacataa cttgtaagga ttccagtggc aatgaaacac attttactgg 180
gaacgaagtt ggttttttca agcccatatc ttgccgaaat gtaaatggct attcctacaa 240
agtggcagtc gcattgtctc tttttcttgg atggttagga gcagatcgat ttaccttgg 300
ataccctgct ttgggtttgt taaagttttg cactgtaggg ttttgtggaa ttgggagcct 360
aattgatttc attcttattt caatgcagat tgttggacct tcagatggaa gtagttacat 420
tatagattac tatggaacca gacttacaag actgagtatt actaatgaaa catttagaaa 480
aacgcaatta tatccataaa tatttttt 508

<210> 246
<211> 358
<212> DNA
<213> Homo sapien

<400> 246
aaatgttggc attcaaaacc aaagatataa ccgaaaggaa aaacagatga gacataaaat 60
gatttgcaag atgggaaata tagtagttta tgaatgtaa ttaaattcca gttataatag 120
tggctacaca ctctcactac acacacagac ccacagctc tatatgccac aaacacattt 180
ccataaacttg aaaatgagta ttttgcatac ctcaagttag gatattgttt ttacaagtta 240
atcctaaagt cataaagcaa gaagctattc atagtacaag attttatttg ctaagcttta 300
caaattaaac tctaaaaaat tattacaatg atactgaaag atattttatt gccctttt 358

<210> 247
<211> 673
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(673)
<223> n = A,T,C or G

<400> 247
gaagaaagtt agatttacgc cgatgaatat gatagtgaat tggatttttg cgtaggtttg 60
gtctagggtg tagcctgaga ataggggaaa tcagtgaatg aagcctccta tgaaggcaaa 120
tacagctcct attgatagga catagtggaa gtgagctaca acgtagtacg tgcgtgttag 180
tacgatgtct agtgatgagt ttgctaatac aatgccagtc aggccaccta cgggaaaaag 240
aaagatgaat cctagggctc agagcactgc agcagatcat ttcatattgc ttccgtggag 300
tgtggcgagt cagctaaata ctttgacgcc ggtggggata gcgatgatta tggtagcgga 360
ggtgaaatat gctcgtgtgt ctacgtctat tcctactgta aatatatggt gtgctcacac 420
gataaacctt aggaagccaa ttgatatcat agctcagacc atacctatgt atccaaatgg 480
ttcttttttt cgggagttagt aagttacaat atgggagatt attccgaagc ctggtaggat 540
aagaatataa acttcagggt gaccgaaaaa tcagaatagg tgttggtata gaatggggtc 600
tctnctccg cggggtcnaa gaaggtggtg ttgangttgc cggnetgtta ntagtatagn 660
gatgccanca gct 673

PCT/US99/30909

```
<210> 248
<211> 149
<212> DNA
<213> Homo sapien
```

```
<210> 249
<211> 458
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(458)
<223> n = A,T,C or G
```

```
<210> 250
<211> 374
<212> DNA
<213> Homo sapien
```

```
<210> 251
<211> 356
<212> DNA
<213> Homo sapien
```

<400> 251						
aaagatcttc	tctaacaagc	tatgggaatt	tggcttcata	ctctttcttt	gcaacagcag	60
tgttctgggt	gataattttg	aattgatacc	tgttcctttt	tctgggtttt	gttgyccttt	120
tgaaaaattg	ctcttccctta	tcattgggtg	gaggcttggt	agcaaagtaa	catttttttg	180
aaaagaggac	agaaaaattg	aactacagct	tgagaacgta	ttcttttttt	ctcacttttg	240
tattggcaat	tgaggaaatca	cttttaactg	ttttagggtg	tggtgtccag	agtgagcaag	300

PCT/US99/30909

356

356

<400> 252

<400> 253

<220>

<400> 254

```
<210> 255
<211> 225
<212> DNA
<213> Homo sapien
```


PCT/US99/30909

```
<220>  
<221> misc_feature  
<222> (1)...(225)  
<223> n = A,T,C or G
```

```
<210> 256
<211> 544
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(544)
<223> n = A,T,C or G
```

```
<210> 257
<211> 420
<212> DNA
<213> Homo sapien
```

```
<210> 258
<211> 736
<212> DNA
<213> Homo sapien
```

<400> 258
aaacaaaatg ctaaacctaa aaacattggt ctgtcagttc ccaaattaaa tctacttaga 60

```

acaaaaacaa aaatttatag ctcggtcaca tactacttaa ataatttgt tcaggcatct 120
ctaaaatcct ccatgttttc aagtatggaa atagaactca aatattccac aatacagtac 180
taaacagatg gagtatttag gaaagacttt gttgtcatat ggcacaatat taatattttg 240
ttgcttcaat acgttttgaa ataaatatca gatttttgtt ttttttctct aaaagaccaa 300
aattataatc tacattaaga taattctgac tgtggttaag acttaagagt gtaaaataca 360
acatcaatat tttatcacia aagtaaagct ggtaacaaat tataaaaagga gccagtaact 420
tactgagaca ggctcggaga ttaaagctca tcatgataga aatagtcac atggagctgt 480
ctgccataat ctgtggcttc actggtgaga aacaagtcag gggtttccag aatctcttct 540
tcagagagct tttgtgcacc attcaaacc atttcatcaa ttagatgaag cgctcctct 600
tgtgcaatgc cctgattatt aggtctaccc aaggtaacag ctcttgggga tcaagcctgc 660
catcggtatc tttgtcataa tcattcaccg aatctgtctt tctcacaagt atcccattct 720
ggatcttcat ttgcag 736

```

<210> 259

<211> 437

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(437)

<223> n = A,T,C or G

<400> 259

```

aaaaccatac tgaaatcatt taccaaataa cnaagatctt aatctaaaag atagtgaata 60
catcatcatc atgaaatctg gttttatgtg ctctatgaag tacttggaga attgcttttt 120
tatttttctt ttgctttatt aggtcacaca aaacagaatg aattagcaga aaaatgtatg 180
ttataaaaca gcatttacta cttcaattta atttttttta ctaacaattg tggacctttt 240
tgatgacact tatgtatggt ttaataaaat tatgtactta ttagtactta atgagccctt 300
cctgcctcaa tataaaatta ctaaaacttg agaattacag attttattgt aggccctgat 360
gttagtcact ttggagaagc taaaaatttg gaaatgatgt aattcccact gtaatagcat 420
agggattttg gaagcag 437

```

<210> 260

<211> 592

<212> DNA

<213> Homo sapien

<400> 260

```

ttttttttt gaaaaatata aaattttaat aaaggctaca tctcttaatt acaataatta 60
ttgtaccaag taattttctt taaatgaact ctttataatg cataatttac agtataagta 120
gaacaaaatg tcatgacaaa agtcattgag tacaagactt gtaataaaaa ggcataaaat 180
atattttatac ataaaccctt ttcaaaaaac aagggaagc ttgagccctc aatatagggc 240
gacacacgga gcgggtgacc gtgcaggtag aggtactgta ctgattttaa gtcaagcact 300
agagatagtg gattaatact cttttgccgt acactatata cagatgtata gtacaagtaa 360
caatggcaaa cagaatgtac agattaactt aacacaaaaa cccgaacatc aaaatgaagg 420
tgtgtggagg aaaggtgctg ctgggtctcc ctacaactgt tcatttcttt gtggggcagg 480
gggtagttcc tgaatggctg tggccaatg actaatgtaa aacaaaaaca gaaacaaaaa 540
aaacaaggaa ctgtcatttc cacgaaagca cagcggcagt gattctagca gg 592

```

<210> 261

<211> 450

<212> DNA

<213> Homo sapien

WO 00/37643

PCT/US99/30909

81

<400> 261

gtggcagggc	ccagccccga	accagacaag	ggacccctca	aggagcttca	ttctagcatg	60
agaaaattga	gaagtaaacc	agaaagttac	agaatgtctg	aaggggacag	tgtggggagaa	120
tccgtccatg	ggaaaccttc	ggtggtgtac	agat+++tca	caagacttgg	acagatttat	180
cagtcctggc	tagacaagtc	cacaccctac	acggctgtgc	gatgggtcgt	gacactgggc	240
ctgagctttg	tctacatgat	tcgagttttac	ctgctgcagg	ggtggtacat	tgtgacctat	300
gccttgggga	tctaccatct	aaatcttttc	atagcttttc	tttctcccaa	agtggatcct	360
tccttaatgg	aagactcaga	tgacggctct	tcgctacca	ccaaacagaa	cgaggaattc	420
cgtcccttca	ttcgaaggct	cccagagttt				450

<210> 262

<211> 239

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (239)

<223> n = A,T,C or G

<400> 262

taactttgat	gacaaaatct	aaaattaaag	anttagtctt	aaaagcctat	agtgacttgt	60
ttacttgcac	aaataatatt	ttcacttagt	acaggctatt	aatataagta	atgagaattt	120
aagtattaac	tcaaaaaaag	atagaggctc	caaacttttc	taagaaatta	atgcattttc	180
aaagtaataa	tataatcaat	ctgttagtca	aaagtaattt	catattcatt	gccaaattt	239

<210> 263

<211> 376

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (376)

<223> n = A,T,C or G

<400> 263

aaaaaaaaa	aaaaaaaaatt	ccttgtngtt	tnttagagga	aaaaaagaaa	aaccccaact	60
tttancactg	atactacata	ttgctctgtt	aaagaatttt	ctctgccaaa	aaaaagaaaa	120
aacaaaaaaa	cgtttaaagc	tggagtttga	cattctgctt	tcagatgctg	tctttttatt	180
agtgagtgat	gatggtttgc	taataatcaa	taggtaataa	ttttttgtaa	tcccatcaag	240
tggctccata	tgtttctgct	ctctcgtgac	tgtgttaatg	tttaactgtt	gtaccttaaa	300
gccgaaatca	gtaactatgc	atactgtaac	caaggatttg	ggcttacaga	gttgttttgt	360
gnataaagaa	aatttt					376

<210> 264

<211> 207

<212> DNA

<213> Homo sapien

<400> 264

aaattagcat	tccacaaata	tacaggtaat	tttaataatta	ttgtgcatga	atacatcac	60
aatgcttata	tatacaaatt	ccagtttgtt	ttcatgtgct	ggcaagggat	ttgtatacaa	120
tcataagctg	tgttcatatt	ggccccattg	aatattcaca	atacaaaagc	acaaaagaac	180
cattgattta	caaaaggaaa	tctattt				207

PCT/US99/30909

```
<210> 265
<211> 388
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(388)
<223> n = A,T,C or G
```

<400> 265						
naactgcact	ttatttggtta	ctgtaacatt	nttttttaa~	tgatcaacca	taagcatgca	60
aaagnccnct	gaaactgctt	ccactgcctg	ttgtatagaa	atgggtaaat	tataaagggtg	120
attcaatttg	gagctccttc	cttttttata	gcacttctaa	gctgtgtgcg	cyacacacac	180
cacagaggta	ggaaggacca	cctttaataa	attatcttct	taatcgcaga	gaatttctga	240
agataaaaat	gacaaaaatgc	taaaccaagg	ctttgatygag	tcccaaaagg	ccacagatcc	300
atcggctcct	atttgaagaa	ttcatccctt	gtagtgttct	agcctttgta	gggcactgga	360
ttacaagatc	caccagggct	ctgaacaa				388

```
<210> 266
<211> 616
<212> DNA
<213> Homo sapien
```

```
<220>  
<221> misc_feature  
<222> (1)...(616)  
<223> n = A,T,C or G
```

<400> 266						
aaatacagag	tcaaaagatg	atttataaaa	tntaaaacat	tttctgcttg	gccgtatttg	60
aagacaagct	gaatacatat	ctatgtttctg	aataagtcca	ctatggatat	atataggaag	120
agatacatat	atatccatcc	acagatacac	acacacatat	atattttctgc	atgtatatat	180
acataaattct	ttctatagtt	acaggaataa	ctctttctat	aattctgatt	ttgactccca	240
tcttccacca	tttactcatc	cactcattac	ctaaatcttg	gctttctttc	ctatatgtta	300
aataatccat	ccaaactttct	agccagtact	gtcaggaggg	ttcttgctcg	agtgagctgt	360
taatactatt	ttccactgac	aactttctgca	catcgaggac	acagtgtatc	tgaagactcc	420
gctgtatact	tccaacaacg	ggggcatttt	tctttcgtag	tcggcattgac	aattacttta	480
taggaagact	cttcacgaat	atcaccacct	tctaagttga	tgaggaattt	ccctttaagc	540
tcgattacat	cttcagctcat	ctctcgtggt	tcttgaccag	taaagttgac	tcagaagcca	600
tcattaattc	attcaa					616

```
<210> 267
<211> 341
<212> DNA
<213> Homo sapien
```

<400> 267						
ccattatgta	tgtattttct	tgaaaaatac	ttatttcagc	tacttatttt	taatagttac	60
ttattcttgt	tgtattgtca	tttgagtttt	gtatatattt	ttgatattaa	ccccttgtca	120
catgtataat	ttgcaaatat	tttctccctt	tttttagttg	tcacattctg	ttcattgtat	180
cagattctgt	gcagcagctt	tttaatttga	agtgatctga	ctgacttggt	cttccttttg	240
tgtcctggga	tatttagggt	aaatcaaaaa	acttgctgcc	cagaccaatg	ttatggggct	300
ttcactctat	tttttggtag	tagtagttta	agagttttag	g		341

<210> 268
<211> 367
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (367)
<223> n = A,T,C or G

<400> 268
ttgtagattg gaatagcaaa agtgaatgct ntgaccaaaa tttttgccct cctaaataaa 60
gacgtntcct tctagagagc aaatctatca taaaatgtca aaactagaag agaataaaat 120
gaaaggaaaa aacctagaaa aatatacctaa aatatcaaat gcagtcattt ctaaataataa 180
gccataatta tagctttacc tattgttctt attgttccta tgctgcttct acaatgttac 240
atcaactata cttagcttta ctctcccaaa atcttggtga tgaagccttc tgagtgtgct 300
ttccaatgtg ccagaaccag aagggcattc caaggcttcc ccacatttcc tccatttacg 360
gagacag 367

<210> 269
<211> 270
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (270)
<223> n = A,T,C or G

<400> 269
caaattcttc cctcactaga cgtaagcctt ttntctactc tctcaatctt atgcatcata 60
gnaangcngn tgaggtggat taaaccaaac ccagctacgc aaaatcttag catactcctc 120
aattaccac ataggatgaa taatagcagt tctaccgtac aaccctaaca taaccattct 180
taatttaact atttatatta tctaactac taccgcatcc ctactactca acttaaaact 240
cagcaccacg accctactac tatntcgcac 270

<210> 270
<211> 368
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (368)
<223> n = A,T,C or G

<400> 270
ctgaatcatg aataacacta tataatagag tntaaggaac acaagcatta gatgtgatcc 60
ttgccccata cccttagatt atgtcagact aaagctgaca attctgccag gctctgaacc 120
cctagtgcc ccaacccaaa tcttggaagc aaagaatatg ccctgtcata caactttgta 180
caagttgtag taaaacaaag cttaagtttt ctcatcttcc tacagcaaataa ggtcagttat 240
ttaataaaca ctaaaatgct cctaagaatc cattttgagt ttgtttacca aacacattgt 300
gcaagaactg actacacaaa aggttccttt gaaatttggg ccacaaattc acttaagggt 360
ggaaattt 368

<210> 271
<211> 313
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (313)
<223> n = A,T,C or G

<400> 271
aaatttatat aaaactctgt acatgttcac tttattattg cataaacagc ataatcttca 60
agacaaanngt ttgcaaacac atgtccaatt caggaaaaaa aatttcacgt ttctcgtctg 120
gcttttttct tcttttttat ttgtttggga gattcccagc tagtttcaga cttgggtctgt 180
gaaggaggca cactattttg cttgggtattt gacttggatt tatctgtctc ttgtagtatt 240
ggcggcactt gggaagagct cttgtcagaa tcactttttg ataagattac agatggctcg 300
gtagaagtag cag 313

<210> 272
<211> 462
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (462)
<223> n = A,T,C or G

<400> 272
aaaaaacatt tattttaata agactattgc naacacatta aaaaaactaa atagtaatat 60
tacaaaatct atataacttg acatttagta tttgtcaatg tgccagaggt tttcttcatg 120
aaatttgact tctttgaaat gaaggctttt ttctatcatc tcttatagct ctgactgaat 180
aagtcttaat gctttcttca tgttttctat caataggggt aaatcccag gctcatatgt 240
gtacaatctg ttagagtatc ttccagctat gtcagctcta actgttaaag aagggtctac 300
aaacatgatt ctaggcacat attgcccac aggtgataaa ttcttatcag tggtttcatg 360
cataagggtt agcatgatga acttatcttg agccatttct tgtatttctt cattttgggc 420
aaatactttc tttagtgtt gagagtattg acaatcctcc ag 462

<210> 273
<211> 282
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)... (282)
<223> n = A,T,C or G

<400> 273
ctgatcaaag catgggatat ttaatatagn ttatacataa tatttttaca tagaaaactt 60
tacatnnat ttcatattat ataattctgc ttattctttc aaaaatttat acatccattg 120
ggcaaggaaat ggttttcatt aaattaccaa tattaaatgc acttaatcat tgtgtatagg 180
ttaaaccaaa gtaactatta actaactttt aggcatttta aggaggtaaa acatacattt 240
tacacataag tatttgatgc aaatatgcag ataaaatttt tt 282

WO 00/37643

PCT/US99/30909

85

<210> 274
<211> 125
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(125)
<223> n = A,T,C or G

<400> 274
cagccctaga cctcaactac ctaaccaacn ttncctaaaa taaaatcccc actatgcaca 60
ttnaatcnct ccaacatact cggattctac cctagcatca cacaccgcac aatcccctat 120
ctagg 125

<210> 275
<211> 528
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(528)
<223> n = A,T,C or G

<400> 275
aaagctgtgg aaaagcttta ttatagattt ttntacagaa ttaaaaaagt tcaaacaata 60
ataagccngg aaccacaaat aattaaaagg aaacacagca atcccataaa caagcattct 120
ggcatctgtt agaaattttc cctcaaatta tgaaatgtag ctctccatgc ttccaatga 180
ttgttataat acccacaaat atctgtgatt tcagtggaa actttaacaa aagttttctt 240
tttaaggcat gatcctgatt cattttttct tcaatatctc agtcatttca ggaactacct 300
taaataaatc tgcaactatt ccataatctg ccacttggaa aattggagct tctgggtctt 360
tattaattgc cacaattgtc ttgctgtctt tcatccagc taaatgttgg atggctccag 420
atattccaac agcaatataa agttctgttg ctactatttt tccgtctgn ccaacttgca 480
tgtcattggg aacaaagcca gcatcaacag cagcacggga agcaccaa 528

<210> 276
<211> 420
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(420)
<223> n = A,T,C or G

<400> 276
aaatgtcttg ttccagat ttcaggaaan ttttttctt ttaagctatc cacagcttac 60
agaaacctga taaaatatac ttttgtgaac aaaaattgag acatttacat tttctcccta 120
tgtggctgct ccagacttgg gaaactattc atgaatattt atattgtatg gtaatatagt 180
tattgcacaa gttcaataaa aatctgctct ttgtatgaca gaatacattt gaaaacattg 240
gttatattac caagaccttg actagaatgt cgtatttgag gatataaacc cataggtaat 300
aaaccacag gtactacaaa caaagtctga agtcagcctt gggttggtt cctagtgtca 360
attaacttc taaaagtta atctgagatt ccttataaaa acttccagca aagcaacttt 420

<210> 277
<211> 668
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(668)
<223> n = A,T,C or G

<400> 277
ccagggtggc tctgatatag cagccctggg ntattttcga tatttcagga agactggcag 60
atngcaccag accctgaatt cttctagctc ctccaatccc attttatccc atggaaccac 120
taaaaacaag gtctgctctg ctctgaagc cctatatgct ggagatggac aactcaatga 180
aaattttaaag ggaaccct caggcctgag gtgtgtgcca ctacagagact tcacctaact 240
agagacaggc aaactgcaaa ccatggtgag aaattgacga cttcacacta tggacagctt 300
ttcccaagat gtcaaaacaa gactcctcat catgataagg ctcttaccoc cttttaattt 360
gtccttgctt atgectgcct ctttcgcttg gcaggatgat gctgtcatta gtatttcaca 420
agaagtagct tcagagggtg acttaacaga gtatcagatc tatcttgta atcccaacgt 480
tttacataaa ataagagatc ctttagtgca cccagtgcac gacattagca gcatctttaa 540
cacagccgtg tgttcaaatg tacagnggtc cttttcagag ttggacttct agactcacct 600
gttctcactc cctgttttaa ttcaaccag ccatgcaatg ccaataata gaaattgctc 660
cctaccag 668

<210> 278
<211> 202
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(202)
<223> n = A,T,C or G

<400> 278
aaattgggat cgacggcaac caggggaagn tnctaaactc ctaatctatt ctggatccaa 60
ttngcnaagt ggggtcccat caaggttcag tggcagtggg tctgggacag atttcactct 120
cacgatcagc agtctgcaac ccgaagatgt tgcaacttac tactgtcaac agagttacat 180
gtccccgtac acttttggac cc 202

<210> 279
<211> 694
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(694)
<223> n = A,T,C or G

<400> 279
ctgtacttgg acaaaataag ttaattctat ttgggtgtcc attaaagttt tatgtggcta 60
tgnaccact ggagctaaaa attggctttt aactgtttcc aaatcagaac tagcagagga 120
gagaagtaaa taaagccaat ggcactccct tcagaggctc aaaatgggta gattttgatg 180

WO 00/37643

PCT/US99/30909

87

```
cagatttaac cttagcgagt ttcagtcagt ccatttagat gatcctgtag gttcatacaa 240
atacactgaa ccgttggttt aacttctctt ccttcctcaa agtttatgat aaagagactc 300
atccctgtat tgggagtgac tgacataagt tcagatctgc tcagagtggc tggtaaggaa 360
cacttaaggt cagtcagaaa ataatacaac agacttctca tgtaagcacc gtgactcaca 420
actaagacac tggctgctaa tcctggaata ccgctgtctg aattaacttt agagctgtga 480
tttttctcta aaggaaatat ctctgccaaa gaagtttcca gacagntgct tgggagatcc 540
ttggggaaaa ctggtctttt tgatccggtt ctttcangan taggtngaca aaagaaatnc 600
aaaaaagntc atcccacgcn tttntcacct gggcccagcg gnnctcctcc nggggggggn 660
aaacacangg gactcttccc nggctngct tnnng 694
```

<210> 280

<211> 441

<212> DNA

<213> Homo sapien

<400> 280

```
aaaaaacttc catgcaactt ctggtttatt gtttggcaac tccacatgat aaaaaataaa 60
aaacagccca accgagtttc ggaattaagt actcttctag taagtgattc aaacttgtaa 120
tatttgccac aggactgact tatttattta cttagtagaa gctcttaagt tcacttgttt 180
atcagggcat atacagaagg gtttggttaa actcgatggt aactttacaa ctttctgacc 240
tgggcatga attctcaagt actgtatttc actgtgttgg tgtgtctgat ggaatttcg 300
aygtggtccc acaaaaaatat tttatgtagt gtgccttcaa agagaacatc ttatttctct 360
tcacttatcg tcccacaaag tcacatttgg tgggtggtcag ccaagtcgca tctggtctag 420
ttttactctt gtcccaattt t 441
```

<210> 281

<211> 398

<212> DNA

<213> Homo sapien

<400> 281

```
aaatttgtaa ggtctgaaga atctaaaact gttaatttaa cccttaactt gtgcctagaa 60
actacagcac atataaaaata tgtaaacacc agcctgttgc tgtacttttc tgcttatttt 120
acagcctcaa atatttctca ttatcttgtc acttagttct tcatgtttct ccttctgact 180
tttaataatg gtaataggaa aacaaaaccc aaagcttttc agaacttcag tgtgaggttt 240
cctattttga caagttaact tgtaataact caggttttac gatgtataat ttacctaata 300
gaccaaacta actcatggag atattttgaa ctattattta ggtacaaaact ttataaagaa 360
tgtagtatg tcataaaaata taacattaca gcttatttt 398
```

<210> 282

<211> 226

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(226)

<223> n = A,T,C or G

<400> 282

```
aaaacaatat tctctttttg aaaatagtat naacaggcca tgcatataat gtacagtgta 60
ttacnccaat atgtaaagat tcttcaaggt aacaagggtt tgggttttga aataaacatc 120
tggatcttat agaccgttca tacaatggtt ttagcaagtt catagtaaga caaacaagtc 180
ctatcttttt ttttggtctg ggtgggggag cccaggccga ggctgg 226
```

PCT/US99/30909

88

```
<210> 283
<211> 358
<212> DNA
<213> Homo sapien
```

<400> 283								
aaacaaaaat	actcaagatc	at ttatattt	ttttggagag	aaaactgtcc	taatttagaa		60	
tttcctcaa	atctgagggg	cttttaagaa	atgctaacag	at ttttctgg	aggaaattta		120	
gacaaaacaa	tgtcatttag	tagaatattt	cagtatttta	gtggaatttc	agtatactgt		180	
actatccttt	ataagtcatt	aaaataatgt	ttcatcaaat	ggttaaatgg	accactgggt		240	
tcttagagaa	atgttttttag	gcttaattca	ttcaattgtc	aagtacactt	agtcttata		300	
cactcaggtt	tgaacagatt	attctgaata	ttaaaattta	atccattctt	aataatttt		358	

```
<210> 284
<211> 288
<212> DNA
<213> Homo sapien
```

<400> 284						
aaaactttttg	ttaagaaaaa	ctgccagttt	gtgcttttga	aatgtctggt	ttgacatcat	60
agtctagtaa	aattttgaca	gtgcatatgt	actgtracta	aaagctttat	atgaaattat	120
taatgtgaag	tttttcattt	ataattcaag	gaaggatttc	ctgaaaacat	ttcaagggat	180
ttatgtctac	atatttgtgt	gtgtgtgtgt	gtatatatat	gtaatatgca	tacacagatg	240
catatgtgta	tatataatga	aatttatgtt	gctgggtatt	tgcatttt		288

```
<210> 285
<211> 629
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(629)
<223> n = A,T,C or G
```

<400> 285						
cctaaaagca	gccaccaatt	aacaaagcgt	ncannctcaa	caccctactac	ctaaaaaatc	60
ccaaacatat	aactgaactc	ctcacaccca	attggacca	tctatcacc	tatanaagaa	120
ctaattgttag	tataagtaac	atgaaaacat	tctctctctgc	ataagccctgc	gtcagattaa	180
aacactgaac	tgacaatttaa	cagcccaata	tctacaatca	accaacaagt	cattattacc	240
ctcactgtca	acccaacaca	ggcctgtctca	taaggaaagg	ttaaaaaaag	taaaagggaac	300
tcggc aaatc	ttaccccgcc	tgtttaccaa	aaacatcacc	tctagcatca	ccagtattag	360
aggcaccgcc	tgcccagtg	cacatgttta	acggccgcgg	taccctaacc	gtgcaaagggt	420
agcataatca	cttgntcctt	aattagggac	ctgtatgaat	ggcttcacga	gggttcagct	480
gtctcttact	tttaaccagg	gaaattgacc	tgcccgtgaa	gaggcnggca	tgacacagca	540
agacgagaag	accctattgga	gctttaattt	attaatgcga	acagnacct	acaaaccca	600
caqgtcctaa	acctacccaa	acctcgga				629

```
<210> 286
<211> 485
<212> DNA
<213> Homo sapien
```

<400> 286
aaatgtactt gctcagctca actgcatttc agttgtatta tagtccagtt cttatcaaca 60

PCT/US99/30909

ttaaaccta	tagcaatcat	ttcaaatcta	ttctgcaaat	tgtataagaa	taaagttaga	120
attaacaatt	ttatttttga	caacagtggg	attttctgtc	atggataatg	tgcttgagtc	180
cctataatct	atagacatgt	gatagcaaaa	gaaacaaaca	aaagccagga	aaacactcat	240
tttcgccttg	aatatgtaaa	tgggattaat	tttgtcctgt	gccttatgtg	gaaaggaact	300
tctttggttt	tccttttttg	ttctggtgga	agcatgtgca	ggagacatat	catccaaaca	360
taaacattta	aaatgtttgt	ggtttgcttg	gctgtaattt	tcaaagtagt	taattgagga	420
caaagggtta	tgcagaagtg	atagctttgg	tttgctgagt	cttgttttta	gtggccttga	480
tatttt						485

```
<210> 287
<211> 340
<212> DNA
<213> Homo sapien
```

<400> 287							
cctggagtc	cc	aataaccacc	ccctcatacc	acaccctgtg	catacaccag	ccaagccttt	60
cctgggtctg	g	gaaggggaaga	gaaaaaagac	gcaggccacc	tgggggttct	gcagtccttg	120
gtcagtc	cag	ccttctatct	tagctgcctt	tggcttcgc	agtgtaaacc	ttgcctgcc	180
ggaggcagga	g	ggcccagctg	gacctccgag	ggccatgagc	aggcagcagc	catcttgcc	240
tcaagcttgc	t	ctttcccttg	agtcctcttc	tcccttcggc	tctagccaga	ggtgtagcct	300
gcagatccta	g	gaaggaaga	gctggggagg	aggatgaagg			340

```
<210> 288
<211> 290
<212> DNA
<213> Homo sapien
```

<400> 288						
aaacagtc	tcctcggt	gtctcctt	gttcaaaact	gttctccc	agattctc	60
gacagcat	accagaac	caagcctt	gtcaatgg	atccactg	agagcaact	120
cgcaattt	tccttcgt	ctcttcag	tctaccc	aggtgttt	atgtgtttt	180
tacggcgt	gataaagt	caagctct	ccaatct	ctgtcttg	gtagatttt	240
cttaaaa	gaagagaa	tcacaaag	acttcct	tcctccaa	agcctgttg	290

```
<210> 289
<211> 404
<212> DNA
<213> Homo sapien
```

<400> 289						
ccacccacgc	ttaggttccc	atcacactga	tgactcgggg	tttggcgagc	acaggagcgc	60
aaaccttttc	acattctttc	tgtgatccaa	atttgttttc	gtttccacca	caacctccat	120
accagaatct	tgcacagctt	ttggtgtttg	gatcatagta	ccattttaat	atgaaatccc	180
tgcaagttcc	ttcgtctttc	ggcaacttgc	atatactctg	ttcagtgaga	gccaatggtt	240
ctgtgctcac	cattagattg	atgggtgaac	tgaagctga	ccttgctggc	tgtggaggtg	300
ggggctgaga	ttctcttgta	ctgaaacttc	cgtggtagg	ggctctgacc	tgagacctca	360
ggtagcagac	cacagccaca	tggatatgtc	gcccagcgag	cagg		404

```
<210> 290
<211> 384
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc feature
```

<222> (1) ... (384)

<223> n = A,T,C or G

<400> 290

ccaggcgctc	cttgtcggca	tcaggagggg	tggccttgaa	ctgctcatgg	gctgtgggtca	60
gtccctggat	ctcctcaatg	gtgtgcacaa	tgaagggtgc	ctgcagggtcc	tccatggccc	120
cctccatcca	gttgttgaag	ggtgcagccc	gcttggcata	ctccaagtac	agctgggtcaa	180
tggtctccag	cagtttctcg	gtccgctcca	gagcttccct	tcgcttctga	gttagggccc	240
ccagattgtc	ccactgggtca	cagatctttt	ggcaacgggc	gttgacactg	ggtgagtcac	300
aatantccag	ctcattgagc	tcctgtgcga	tggcggcaat	ctgctccaca	cggtcctggt	360
gggcagccag	gccactctcg	aagg				384

<210> 291

<211> 278

<212> DNA

<213> Homo sapien

<400> 291

aaagtttatt	tttacrattt	ctttatcact	ttattgtatc	atcaccattg	gtttcataat	60
gtaaatacta	tatgttgaac	aaattaaatg	tcaaaatttt	ttattaccat	agtcacatgtt	120
aatagtgggg	ctttcagggtg	tttagagatt	ttttttgttg	ttgttaacat	tcattgcaaa	180
agtactagat	ggtgtataac	tctagagttg	aattttaagg	gattccctaa	tatgtatact	240
atctttttat	ctgaagtaat	aaataaacia	tgatcttg			278

<210> 292

<211> 177

<212> DNA

<213> Homo sapien

<400> 292

ccttgggcccg	gtcattcttg	tccagtttga	taggttcagg	aaattcgttg	tacagctcca	60
cctccgtttc	ctgcttaagt	gcattccgtg	caatcgtctg	gaacgcctgc	tccacgttga	120
tggcctcctt	ggcactggtc	tcaaagtagg	gaatgttggt	tttgctgtag	caccagg	177

<210> 293

<211> 403

<212> DNA

<213> Homo sapien

<400> 293

aaaaagaagg	acttaggggtg	tcgttttcac	atatgacaat	gttgcattta	tgatgcagtt	60
tcaagtacca	aaacgttgaa	ttgatgatgc	agttttcata	tatcgagatg	ttcgctcgtg	120
cagtactgtt	ggttaaatga	caatttatgt	ggattttgca	tgtaatacac	agtgagacac	180
agtaatttta	tctaaattac	agtgcagttt	agttaatcta	ttaatactga	ctcagtgtct	240
gccttttaaat	ataaatgata	tggtgaaaac	ttaaggaagc	aaatgctaca	tatatgcaat	300
ataaaatagt	aatgtgatgc	tgatgctgtt	aaccaaaggg	cagaataaat	aagcaaaatg	360
ccaaaagggg	tcttaattga	aatgaaaatt	taattttggt	ttt		403

<210> 294

<211> 305

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(305)

<223> n = A,T,C or G

<400> 294

aaagcaatct ggcattggtgt cctgtagtga agcagaggat cataacataa gtaaactctc	60
tatgggtgga agttggagag aaggacattt tggctttgt catgaaaaga ctctccagat	120
agaaacagat tctgcccata agtgaaataa aatgctttgt gggggtaatg agtgacttat	180
agtattcagg cagatgttac ataactgcta attaagtttc cctggattga ntttanncaa	240
anaattgaaa gtngattttg gtcangtgtc agnaaactac tgcctataaa cccatatcnt	300
accca	305

<210> 295

<211> 397

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(397)

<223> n = A,T,C or G

<400> 295

cctatctggt tggccttttt gaagacacca acctgtgtgc tatccatgcc aaacgtgtaa	60
caattatgcc aaaagacatc cagctagcac gccgcatacg tggagaacgt gcttaagaat	120
ccactatgat gggaaacatt tcattcccaa aaaaaaaaaa aaaaaaaat tctcttctt	180
cctgttattg gtagttctga acgttagata ttttttttcc atgggggtcaa aaggtacctt	240
agtatatgat tgccgagtgg aaaaataggg gacagaaatc aggtattggc agtttttcca	300
tttncatttg tggnggaatt tttaatataa atgcggagac gtaaagcatt aatgcnagtt	360
aaaatgtttc agtgaacaag tttcagcggg tcaactt	397

<210> 296

<211> 447

<212> DNA

<213> Homo sapien

<400> 296

ccatcctcga tgttgaagtt gtcgtggggc ccgaagacgt tgggtggggat gacagcgggtg	60
aaggtgcagc cgtactgctg gaagtaggcc ctgttctgca cgtcgatcat cctcttgga	120
tacgagtacc caaaattgct gttgtgggga ggccattgt ggatcatggt ctcactatc	180
gggtaggtcg tcttgtcagg gaagatacag gtggacaggc aggacaccac cttgcgggcg	240
cccacctcga aggcggagtg caggacgttg tcgttcatgt gcacgttttt cctccagaag	300
tccaaattgt atttgatatt ccggaacagg cccccacca ttgcagcaag atggatgacg	360
tgtgtgagtt ggaccttctc aaacagggcg cgggtctgtg ctgtatccgt gagatcggcg	420
tcttttagagg agacaaacac ccagtcc	447

<210> 297

<211> 681

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(681)

<223> n = A,T,C or G

<400> 297

aaataacagc	atgtaaaata	ttaaaatata	agctttcaaa	aataaatata	taaataagta	60
gaaccctcgt	aagaaatagt	caaacacatt	aagtcctttc	cagctgtccc	tagaaagctg	120
ctgttctctt	tttcattttc	agctctggta	agggcagggg	ccaccctgca	ggaagtgtca	180
atgatacget	gataagcttc	ttactttctt	cctgtcagtt	ggtgctcccc	ctgtgatgag	240
aaaagggtta	ctgttgacag	tgctaaggaa	ggctgctctt	ctgtcactct	gaagttgctt	300
ggagggatgt	ccccatgcag	actctctccc	agccctccac	tcagggaagg	tctgtctgta	360
cccactgcct	tctatagcag	aaaacttgca	ctcctgaatg	cttttttttt	ttttcaagaa	420
agaagnggct	gnggactcaa	ctagattctt	ggtttgaaaa	agccaaaaca	tattggtcac	480
tgattgtcac	attgggttag	aaatgtccat	tcatgatctc	ccttaagctg	cacacaaccc	540
tatgaaataa	ctaccattat	ctaccctatt	ttgctaaaagc	tcaaagagat	taaataatgt	600
tgacagggat	cttagccttg	aactcactga	agnggttact	gcaaagttct	gctcttcacc	660
aagaaggntt	acaggccaaa	g				681

<210> 298

<211> 353

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (353)

<223> n = A,T,C or G

<400> 296

cctggcttaa	gaccagacat	ttgaagaagg	ctccaggcag	ggaaaggaaa	ggagaggcca	60
gccccacnct	gnccctctcc	tgccccacag	tctccagcaa	cacaaggcgg	ccagtggacc	120
gtgaaccatt	tattttccaaa	ctataaagaa	acctgctctc	tgagaaaaana	cactgcccag	180
gngatgaagc	tccagccctt	ggaggtccaa	aaccacagtc	aaactcagtc	cctttagaaa	240
gctgctgtgc	cttggaatg	annntcggnt	gtcanagcct	gggaagtgg	gggaagaacc	300
agcccaactcc	cctctcctgc	tgcgattcca	gcgcncggtg	ggncagatc	tgg	353

<210> 299

<211> 560

<212> DNA

<213> Homo sapien

<400> 299

aaagttcaag	gactaacctt	atatttttgg	gaaaggggag	gaggaaggaa	atgatatggt	60
accagacac	tgggctaggc	tgcaacttta	tctcatttaa	tactcccagc	tgtcatgtga	120
gaaagaaagc	aggctaggca	tgtgaaatca	ctttcatgga	ttattaatgg	atttaagagg	180
gcatcaatca	gctcaactca	agattttcata	atcattttta	gtatttagat	tgtgcctcaa	240
agttgtagta	cctcacataa	cctccactgg	tttctgtttg	taaaaacctt	cagtgaagttt	300
gaccattgtg	ctcttggtct	ttgggctgga	gtaccgtgg	gagggagtaa	acactagaag	360
tcttttagtac	aaaactgctc	tagggacacc	tgggtgattcc	tacacaagtg	atgtttatat	420
ttctcataaa	gagtcttccc	tatcccaagg	tcttcatgat	gccagtagcc	atatatgata	480
aattatgttc	agtgataact	tagttatcag	aaatcagctc	agtggctctc	cccgccatga	540
ttcacatttg	atgagttttt					560

<210> 300

<211> 165

<212> DNA

<213> Homo sapien

<220>

PCT/US99/30909

93

<223> n = A, T, C or G

```

aaaaactaca taggggtgtg tgtgtgtgtg tatgtttatt ttatacacac atatttgtat      60
attctaatat attactaagg caattttaat gaattacat  gtatataaaa aaatatctgn      120
cacttggcac acaggtttgt atgtatgtgt atatatatat gtatg                        165

```

<213> homo sapien

aaaatatatg	tattttaaaaa	caaaaagcaa	cagtaatcta	tgtgtttctg	taacaaattg	60
ggatctgtct	tggcattaaa	ccacatcatg	gaccaaatgt	gccatactaa	tgatgagcat	120
ttagcacaat	ttgagactga	aatttcagta	actatgttct	aggtcagttc	aacagtttgc	180
ctgctgtatt	tatagtaacc	attttctctt	ggactgttca	agcaaaaaag	gtaactaact	240
gcttcacatc	cttttgcgct	tatttggaaa	ttttagttaa	agtgtttaac	tggcatggat	300
taatatgagt	ggagttttat	ttttaagaaa	aattcacaag	ctaacttcca	ctaattccatt	360
atcctttatt	ttattgaaat	gtataattaa	cttaactgaa	gaaaagggtc	ttcttgggag	420
tatgtttgtc	taaacattt					438

<213> Homo sapien

```
ccaaaacagg agtctcgggt gatatcatca tgagaccacag ctgtgctcct ggatgggttt 60
accacaagtc caattgctat ggttacttca ggaagctgag gaactgggtct gatgccgagc 120
tcgaagtgtca qtcttacgga aacggagccc acctggcatc tctcctgagt tt 172
```

<213> Homo sapien

ccagcctggt	gcaggtgct	tcagcggg	cgctggctgc	ggacttcct	tccgggtct	60
ggatcttttc	atcctaccag	atgagaaagg	gaatgagtga	atggagtgc	ccgcaccct	120
gtcactttcc	tgagacatga	ctgccaggaa	gaagagctgc	tctggtctcc	atcagggtcg	180
gcaggacaaa	ctgaccagtg	agtcagttag	cagagttcac	actgaaaaag	ggcacaaggg	240
ctgtcccaca	atgggaggaa	atgggggtctc	agaacttcta	cttctctgaa	aactaagaca	300
caattggggac	aaccaccacc	ccggtgtgag	atttctcacc	tcgagacagg	acaagatgaa	360
gttcacggct	tcttctgggg	taaagacctt	gaagagccca	tcacaggcca	acaaaatgaa	420
cctacaacac	cagggagaaa	tataaacggg	ttttaggccc	aacaaaaaaa	taaaaaataa	480
aaaaagggcc	tgagatgga	gataaaataa	atatttgtcc	aactattcaa	aggctaagggt	540
tttttttctt	tt					552

<213> Homo sapien

<400> 304

```
cctttgattc ttggtagtag attgcatgta aaatgtttat aagaagctac ttttccttca    60
tggaagaaa tttccacatg agattcataa attcttagac tccgtggctt ctttggtccg    120
gaatgcttaa actcatatga gtgttctgga tccagtgta tccaatcata attcacatta    180
tcaccttcac gaaccacata ctttgccac ggtgaaatac gatacaagat ctctccgctt    240
ttactagtaa taactacctt taatttggat ccatgaggca cgagtacaga tttattctgc    300
tttggtggga tatacagctc ccattttcca taatccagtt ttttgatgg gtacgaaaat    360
ggattccaac cattaaaatc tccagtaaga aaaactcctt ctgctcccgg ggcccattct    420
ttgcagtata aaccaccatc agcacatctg tggacgcaa atgattcata gcctctggaa    480
aacttatcaa taccaccttc attttctcca atgttcttca aaatttggct aaactgctta    540
tacctgcgct ggaagtcac ggctagggc ttcaagtacc ggtcgatctc caggagctctg    600
g                                                                    601
```

<210> 305

<211> 401

<212> DNA

<213> Homo sapien

<400> 305

```
aaataacagc atgtaaaata ttaaaatata agctttcaaa aataaatata taaataagta    60
gaaccctcgt aagaaatagt caaacacatt aagtccttcc cagctgtccc tagaaagctg    120
ctgttctctt tttcattttc agctctggta agggcaggga ccaccctgca ggaagtytca    180
atgatacgct gataagcttc ttacttctct cctgtcagtt ggtgctcccc ctgtgatgag    240
aaaagggtta ctgttgacagg tgctaaggaa ggctgctctt ctgtcactct gaagtgtctt    300
ggaggggatgt ccccatgcag actctctccc agcctccac tcaggggaagg tctgtctgta    360
cccactgcct tctatagcag aaaacttgca ctctgaatg c                                                                    401
```

<210> 306

<211> 313

<212> DNA

<213> Homo sapien.

<400> 306

```
aaactgacta tggattcctt gaaggctctgg cagttgttga tgatggcgat catgtactga    60
acgtagcagt gagggtgctg ccgattcctc aggtgctctt ctttatacag ctgcgcttca    120
tctttatatc tgaggacaga caggcttcgg tcagacagca ctaagggcaa catggagctg    180
tttcaaatgc cacgtgacg tcacgcctgg cctgaaattt cacatcacta acatctgacc    240
ggatgagcct ctaaaaataa aacaatcttt agacgatcca gactaatgga aggacagaga    300
ggttgattac ttt                                                                    313
```

<210> 307

<211> 366

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(366)

<223> n = A,T,C or G

<400> 307

```
aaagatgctg ntaatgaaca ttacggacaa ttcatggtgt ggctagttgg taacacttca    60
gctgattttt cttatgagat ggaaaaaaaa aatcagccaa gtaagggcac atcttcaact    120
catttataag tcagcatcca aggtaaaaga attctctgtt ggacttgaca tcaactcccat    180
```


WO 00/37643

PCT/US99/30909

95

cctctgatac	tcgcctactc	tcttctcaaa	gaagttagnt	ctttccttcc	antgaaatat	240
tctcataaaa	gtcaaattggg	ttctctactc	tgaaaacctt	gctaaaaccc	aattccagca	300
taagtttgtc	tgncacaaac	ncaatgnatt	gcttcattaa	antgcaattc	atcccaatga	360
gcttcc						366

<210> 308

<211> 534

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(534)

<223> n = A,T,C or G

<400> 308

ccagctatca	gctgatcgtc	ttctgtctgg	acgctcgctc	tgcttctgac	atcaaaatct	60
tctgtctcaa	agtcagagtc	atccaactcc	tcaggggtcc	ttatcatcag	caactgctttc	120
ctgatgtccc	ggatgccatc	atataccagg	cggaagcat	cgataaactc	attctcatcc	180
atgggctggg	cagggtccga	gctgagggtc	tccacggctg	cttctacttg	ctcagtaaaa	240
cgtggcatga	ctgtgttgga	gagcagctta	gtggcttcca	gaaccttctc	tgtgtagact	300
cctggctcat	agtcgtccat	ctctgagggt	actacgtgaa	tgacctgggc	tgcccggcct	360
cgaattgcac	cagctgtgcg	gccaggccat	ccacatcctt	ctcttgagga	gcaatgacac	420
atttggctac	atcttccaaa	atgtgattct	ctgagacagc	caagaagtca	tcaatggaag	480
taatgncatc	gacagcatct	gtgagaacac	cgacttggtt	ttccattgnt	cttt	534

<210> 309

<211> 164

<212> DNA

<213> Homo sapien

<400> 309

catactcctt	acactatttc	tcatcaccca	actaaaaata	ttaaacacaa	actaccacct	60
acctccctca	ccaaagccca	taaaaataaa	aaattataac	aaaccctgag	aaccaaaatg	120
aacgaaaatc	tgttcgcttc	attcattgcc	cccacaatcc	tagg		164

<210> 310

<211> 131

<212> DNA

<213> Homo sapien

<400> 310

aaaaatcatt	tatcttttcg	tgcttcaaca	tgatgccaaa	caaaaatcta	ctgaataaaa	60
atagcaagga	agggaatcaa	acatttataa	gatataattt	ttatttttct	gaccaaagtg	120
caatgatttt	t					131

<210> 311

<211> 626

<212> DNA

<213> Homo sapien

<400> 311

cctatgtgcg	ccagttttcag	gtcatcgaca	accagaacct	cctcttcgag	ctctcctaca	60
agctggaggc	aaacagtcag	tgagagtggg	ggctccagtc	agacctcgcc	gacccctggg	120
cacctggcac	tcaagcactt	tgacgatgt	ctcaaccaac	atctgacatc	tttcccgtgg	180

96

<400> 314						
ccagcgcactc	cagcgggtggc	agcaggcagt	gcacgtactc	tgggcctccc	accagggtag	60
tgaagggttcc	cagctgttct	gccaggggcca	ggaggagctc	atcttcatca	tagatggtat	120
ctgtaaggaa	aggcagaagc	tctacttcggg	tcctttcaac	cccaaggggc	aaggcgatgg	180
tggacagctt	cttgatgctg	ttcaggcgaa	gctgaacgtc	ctcatctcgg	agttcgtcta	240
tgcagccgc	cttgggggtac	agcagagtcgt	cgcggtcggc	cgcgcccatc	ttggctccgt	300

WO 00/37643

PCT/US99/30909

97

ccctttcttg tcagactgcg gccagcgctg 330

<210> 315
<211> 380
<212> DNA
<213> Homo sapien

<400> 315
aaaaatgaca ttgcgttttag cttattgtaa gaggttgaaac ttttgtatgt tgtaactatc 60
tttaagccct tcagtttata attcatataa aatgcctttt gtatttaaaa taatcctatt 120
ttaatcagtg catgaaattt gcttttttaa agttcatttg aatgattatt cttccctct 180
aaagaaatga ttttggtaat gttgagaggt accttaccac aaatcctaac tgtaagtgtg 240
ttcatgggtta ttttcaaaaag aattatgact cttccccaaa agaactctaa aaaacttgta 300
ataaacctat aaagctgatt tgcataatga caaaattttg aatagcaaat ataggcaact 360
catatatgta tataattttt 380

<210> 316
<211> 222
<212> DNA
<213> Homo sapien

<400> 316
aaactacaga gggttttcca gctattatgt ccttttagttt craaaaagtaa cgacttatat 60
taatgtttta taaaagatag tgatgaaaaa aaggtaatgc tgaaataaag gcgcttttag 120
aaatatttaa ggacaacata aggtattaat attggaaaaa aactgtacat attttcaagc 180
acaacactga aatattgcag cagtgtttta ctgaattgtt tt 222

<210> 317
<211> 490
<212> DNA
<213> Homo sapien

<400> 317
ccttgaatga gcgtggagag cgattaggcc gagcagagga gaagacagaa gacctgaaga 60
acagcgccca gcagtttgca gaaactgcgc acaagcttgc catgaagcac aaatgttgag 120
aaactgccta tcttggtagc tcttcttaag agaaactgaa gagtttggtc agcagttttt 180
acaagaattc gggacctccg cttgcttctt tttttccaat atttgacac ttagagtgg 240
ttttgttttt tcttttcaga tgtaaatgtg aaagaaaggg tgttgcattt ttacatttcc 300
ctaagtatct tgctaataaa tgctacaata gcatcggtc ctttttgggt ttttgctccc 360
tcccactgtg tgatgtgtg tatatgtatg ttttgaatat gttttcttta ttaaaaaata 420
ttttttgtag tttgaatatg aaatttggac caaatgataa actgcgctga gtctaaactg 480
gcaacatgta 490

<210> 318
<211> 340
<212> DNA
<213> Homo sapien

<400> 318
cctggagtcc aataaccacc cctcatacc acacctgtg catacaccag ccaagccttt 60
cctggctctg gaaggggaaga gaaaaaagac gcaggccacc tgggggttct gcagcttttg 120
gtcagttccg ctttctatct tagctgcctt tggcttccgc agtgtaaaacc ttgcctgccc 180
ggaggcagga ggcccagctg gacctccgag ggccatgagc aggcagcagc catcttggcc 240
teaagcttgc ctttcccttg agtccctctc tcccctcggc tctagccaga ggtgtagcct 300
gcagatctag gaagagaaga gctggggagg aggatgaagg 340

98

<400> 322

PCT/US99/30909

aaaaagaagg	acttaggggtg	tcgttttcac	atatgacaat	gttgcattta	tgatgcagtt	60
tcaagtacca	aaacggtgaa	ttgatgatgc	agttttcata	tatcgagatg	ttcgctcggtg	120
cagtactgtt	ggttaaatga	caatttatgt	ggattttgca	tgtaatacac	agtgagacac	180
agtaatttta	tctaaattac	agtgcagttt	agttaatcta	ttaatactga	ctcagtggtct	240
gccttttaaa	ataaattgata	tggtgaaaa	ttaaggaagc	aaatgctaca	tatatgcaat	300
ctaaaaatagt	aatgtgatgc	tgtatgctgt	aaccaaaggg	cagaataaat	aagcaaaatg	360
ccaaaagggg	tcttaattga	aatgaaaatt	taattttgtt	ttt		403

<400> 323

ccagaattag	ggaatcagaa	tcaaaccagt	gtaaggcagt	gctggctgcc	attgectggt	60
cacattgaaa	ttggtggctt	cattctagat	gtagcttgtg	cagatgtagc	aggaaaatag	120
gaaaacctac	catctcagtg	agcaccagct	gcctcccaa	ggaggggcag	ccgtgcttat	180
atttttatgg	ttacaatggc	acaaaattat	tatcaacct	actaaaacat	tctctttctc	240
ttttttctcg	aattatcatg	gaggtttcta	attctctctt	tgtgaatgta	gatttttt	298

<400> 324

```
ccatgggaag gtttaccagt agaatccttg ctagggtgat gtggggccata cattccttta    60
ataaaccatt gtgtacat                                     78
```

<400> 325

```
ccatcatggt caggaactcc gggaaagtcaa tgggtcccgtt cccatctgca tccacctcat    60
tgatcatatc ctgcagctct ctgttcagtgg gggttctgtcc cagggatctc atcactgtcc    120
ccaactcctt ggtggtgata qtqccatctc catccttgtc aaagagggag aagg          174
```

<220>

```
<221> misc_feature
<222> (1) ... (679)
<223> n = A,T,C or G
```

<400> 326

aaaactgaaa	tacctcttaa	aataatttga	tccccagcgt	ttgctctttt	tgaagtaacc	60
aacttactct	taaaaaggat	ggntgccaa	atggaaagtc	ttactggggt	ttcatgttaa	120
cctattcttt	ggacataact	atgaattttg	tatacaatgc	acttcatgaa	aagttgtggc	180
tccccccagat	tgtccacaag	tgtgactctg	aagtcctaa	catttgtcca	tgtaaagctt	240
aaaacacqct	taactgaqtt	attcaagtag	cagctactaa	agatacaatt	cttgaagcag	300

tttcaatggt ttctgatcca aataatcagt ttctgaacat tactacttca cataatagag 360
tccatcttca gtttcttctc actttctctt tcccttttgg gtttctttt tgtggcctga 420
ggccaccagt tctttgggta ctatcaagat acttccatca tgggtacact ggagagcata 480
gtggttggga ttgactggcc taccttgggc atctcttaat ctactaaaaa tatcatgata 540
aaggtcatgc agtttctggt tcattatggt aatagctttg gtacattgtg cttgctctct 600
cttaanagtt tccttctttg cttgcaagtt acatacatca tcttctaaat tcaaaattat 660
gtccattttg gcgtttacc 679

<210> 327

<211> 619

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(619)

<223> n = A,T,C or G

<400> 327

aaaataagtt actggtaaat ggagttgcat tctatagtc cttataaat attaacaaaa 60
tatttataac tggaacctta atgaaatgta tcatcaaadc aggtaaaaag aacttgctcg 120
cagttaccaa agcctanata cgcgttagat gcgccttttc cggcctgtgc gtctgctctg 180
gttcctctca ggcagcaaag ctggggaagg aagctcagyc aggaagcctcc ccgacgccac 240
aacggcacia gcagcagcta aagcaccgca ctttgcctca ctaacctttt acttaaatga 300
ggttttgcca aatccacatc tggaaccgcy tcacacccat ttgcaaggat gtttgctctt 360
tgatgaaact gcactctctac tgcacatgag ggctttcatt gtaggacaag aggagagttc 420
gtttattttt gtaactgttt tacatgttcc gattagttaa tccgtagctt atgtcatttg 480
ctatgcctgn agncttctaa tctctcctta ctaaaacatt acttcaaatt tgaattgacc 540
cttggttata atttatttag ccgggatttg tgtgtcattg tagagcaact ctaattcaag 600
aatagtgaac acttttaag 619

<210> 328

<211> 132

<212> DNA

<213> Homo sapien

<400> 328

aaatccaaat acaaaagcat agtctctgca agattttggt ctttgaattt cttgatattg 60
taattgatta ttgataactg tcatcatgaa attatctctc aataataaga taaataaact 120
agcatatgaa tc 132

<210> 329

<211> 854

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(854)

<223> n = A,T,C or G

<400> 329

ccttgaggta actattgcaa aatatacagt gtaagttcag tctgatggaa accccagatt 60
catcaaggat acaaacttac agtagcccaa tggcggtttc atagtgtata atttattatc 120
aataaaatta actccgttac aatcagcatt catttctctc aattaaaatt aagcataaac 180

WO 00/37643

PCT/US99/30909

101

cctaggtagt	aaccttctgc	acatatgtat	agctccgaat	ttcctcactg	ttcgtctggt	240
gcaaaaacaa	tattcaagct	tgtctgatta	tgcataat	ctttaatcat	atagattata	300
tatacaatag	acaagacagg	actatataga	taatggacag	acttaaatgc	ccgcattttt	360
aagggtggaga	aaatgatgaa	tctatgcac	cccgagaaca	cttaaaattt	ttttttattt	420
cactgggaaa	ttcttacagc	tactttacaa	tcataggtta	acagcctagt	tatacagaag	480
acataattcca	ctacagagct	atactctatg	caactgtttt	ttcccctcat	aaacaacctg	540
agttcaaatt	gaattctatc	ttccacaatc	acaatgggtg	catcacccag	tacacagaag	600
tttgaatcac	aaaacataat	taccacaata	aaacacagtg	ttcaagtatc	ttggcagagc	660
aatctgccgc	acaaactgca	aattaaatta	actacacaga	ctaaaaacta	tacagcctac	720
catcacagtt	gtgcattata	aaaaagggag	tttctttcct	ttggtttta	gtcaggaaca	780
gggtaggatt	ttttaccctc	nggccgggga	ccacgctaaa	ggggcgaaat	ttcttgccan	840
natattccnt	tcac					854

<210> 330

<211> 299

<212> DNA

<213> Homo sapien

<400> 330

ccaatgaata	actgacttta	taatcctggg	caatcagctt	ttggcggggt	gtaagtgctt	60
ctcgacactt	ttcactcatg	gattcttcaa	atztatgggt	aaagaggcac	ttatacactc	120
tgccctcacc	agcttgtgta	ttttcacaaa	aacgctcccg	atcatctcgg	caagcaaaat	180
ataaatgccg	gtctaagtga	aagtcacccg	atgacagctc	agccaccggg	agaatggctt	240
tcttgccagag	ttcagaaact	tgaatcttgg	gttctctttc	ttctgcttct	ttcaccagg	299

<210> 331

<211> 573

<212> DNA

<213> Homo sapien

<400> 331

aaagatatga	acagcttaat	tttccgtgtg	attatcta	taaaaaagaa	aaacaaaaca	60
agcaaaatgt	tcaagttaaa	aaaaaaacat	accgggtgag	caatgcacta	aaattatcca	120
catgaaaaca	aatgggtctgt	aattcttata	accaacatag	catttcactg	tcaacaatgt	180
gaaaatttaa	tatcttctca	aacaggcata	agatgaagaa	gtgctat	tttaattgtaa	240
aagggaactta	tgtaatgtaa	aattacatta	taatttttca	ttccgaattg	acaaatgatt	300
tcaaaaacaa	ggatcaaagt	ttgactgcaa	atagtaatgc	aatataattt	cataaaaatc	360
cttcaatttc	tatttttttc	cttttctgta	gttgacatat	gaagaccact	tcaatttcta	420
aaaaagggaa	ccattccaat	tttccctccc	caagaaaatg	tctcacaatt	acaaagtaga	480
aaaaacagccg	ttcataaatg	caaaaaaatt	ctgatttata	tatgaaataa	tttctagatc	540
aattcaacat	atttgatgac	atttggtgag	ttt			573

<210> 332

<211> 555

<212> DNA

<213> Homo sapien

<400> 332

aaatttgaaa	gttgtaagca	ctgatgttaa	tgtgattgat	cagcatgggc	atatgtaaaa	60
tgtccttttc	tggttgcctc	tctatgctat	tgtgttcaga	tacttacacc	ataattaaac	120
agtaagttat	agacttgctg	agtttggcat	agatagtgcg	ctcattta	ctgtgcctct	180
caaaacttca	gaatattg	atattaccac	aaataatttt	tggtgaaact	attgagatat	240
taaaattttt	gaaatcacta	ctgttacctg	ttatagaaaa	tagtgttggc	ttagtctagt	300
ctctgtgtaa	ctggttacat	tttgatgggt	gtctatactc	aactggatat	gtgtatgtaa	360
attagaaaat	acatacctat	ccagacataa	atgctaagta	acattttttt	cttctctcaa	420

PCT/US99/30909

```
ctacataatt tgtagctcat catttttcct taatccttcc ctaacttgtc gcagcagttt    480
gaatttccca gatatttatg tttgaacata atgggtcaga atacatatatt gaacatcata    540
gttgtatata ttttt                                     555
```

```
<210> 333
<211> 460
<212> DNA
<213> Homo sapien
```

<400> 333						
aaattttcttt	caacagtcta	ttgggggtcca	aaaagcatat	atcaaaaaca	aaataacaaa	60
agcaaaaaca	aatgctacat	gtaaaagcta	aagaaagaaa	atgcagcata	ttcaggtttc	120
ttttcttgag	gtacctatat	aaatttaatc	acctgcccca	aagtcctctc	gttaggttaa	180
aaacacaatg	cgtcctgggg	agccaattgc	cgggcacgtc	ttattactga	gaaagtgcaa	240
gaatgctgat	catcttatgc	agcatactaa	aggatgattt	actctttaca	aaatagagct	300
taagtatcaa	ccctgatgaa	gttagaaaaa	taaaaacatt	taagtagaat	catctctctc	360
tctatttttg	agatcctgca	gcaaaaagcc	tcccaaatca	actttcaaag	ttctgccatt	420
aaggaatgtt	ggttctcttg	taaaattcag	agatctcttt			460

```
<210> 334
<211> 190
<212> DNA
<213> Homo sapien
```

```

<400> 334
ccaaggaagg ctgtgctcta gccatctga ccctgtctgc aaaccacctg ggggacaagg 60
ctgatagaga cctgtgcaga tgtctctctc tgtgccctc actcatctca ctggatctgt 120
ctgccaaccc tgagatcagc tgtgccagct tggaaagact cctgtccacc ctccaaaagc 180
ggccccaagg                                     190

```

```
<210> 335
<211> 394
<212> DNA
<213> Homo sapien
```

<400> 335						
aaatttggac	agacttctag	cggaagttta	cttctcaaga	attttctata	caaaaagctgt	60
gccaggcata	tattttctca	ccaggacaca	tggggcagcg	gacccttggt	gtcagtaaga	120
acacacccag	aatgatataa	ccagatattt	ttcagtttct	aaattaagyc	atattcaaaa	180
aattccatgt	acaagtttac	accacttttc	taagtacttc	accaggtaat	taaagcagat	240
tcacagatga	attactctca	gttcaactat	atgcaacaac	catgccaaata	acttttcttc	300
tcaattttgc	ataataatgg	ttaaaaaaag	tggtagttta	actatcatgt	tcacaattgt	360
catttttcaa	ggcagtagaa	gaccaagaca	tttt			394

```
<210> 336
<211> 429
<212> DNA
<213> Homo sapien
```

<400> 336						
aaaagctatc	accattgtag	tagaatcatc	cttctttttt	gaaatttgaa	gcaccccagg	60
cttaaaatct	tgtgtttcag	aaacacagtt	tatacatga	ctgcttaatt	atcccccaa	120
agaccttctg	attgaagtca	tgtacagttc	agtgcctaa	attctctgcc	tttttaactt	180
gcttttcaag	cctactctga	aaataagtta	tttagtcaag	ttattctcaa	agatgtccca	240
gttgcttaga	aggatcaaaa	tggaaacattt	gacacacata	ctcaaaaaaaa	tgtaaactgac	300

PCT/US99/30909

```
tataaacact ttaacctaat catctgtatc aaacttttcta aaaatcaaat ctccaggattg 360
ttccacttta gagattctat gtaaagttta tataactata cttgtcaaat agcacctatc 420
tatgcattt 429
```

```
<210> 337
<211> 373
<212> DNA
<213> Homo sapien
```

<400> 337						
aaagatgctg	ttaatgaaca	ttacggacaa	ttcatggtgt	ggctagttgg	taacacttca	60
gctgattttt	cttatgagat	ggaaaaaaaa	atcagccaag	tgggcaca	tcttcagttc	120
atttagaagt	cagcatccaa	ggtaaaagaa	ttctctgttg	gacttgacat	cactcccatc	180
ctctgatact	cgcctactct	cttctccaaag	aagttagtct	ttccttccag	tgaatatattc	240
tccataaagt	caaattgggt	ctctactctg	aaaaccttgc	taaaaaccag	ttccagcata	300
agtctgtctg	ccacaaactc	aatgtattgc	ttcatcagag	tgcaattcat	cccaatgagt	360
ttcacaggca	agg					373

```
<210> 338
<211> 366
<212> DNA
<213> Homo sapien
```

<400> 338							
ccatcccctt	atgagcgggc	gcagtgatta	taggccttgc	ctctaagatt	aaaaatgcc		60
tagccactt	cttaccacaa	ggcacaccta	cacccttat	ccccatacta	gttattatcg		120
aaaccatcag	cctactcatt	caaccaatag	ccctggccgt	acgcctaacc	gctaacatta		180
ctgcaggcca	cctactcatg	cacctaatgt	gaagcgccac	cctagcaata	tcaaccatta		240
accttccttc	tacacttatc	atcttcacaa	ttctaattct	actgactatc	ctagaaatcg		300
ctgtgcgctt	aatccaagcc	tacgttttca	cacttctagt	aagcctctac	ctgcacgaca		360
acatc							366

```
<210> 339
<211> 319
<212> DNA
<213> Homo sapien
```

<400> 339							
ccctccctcc	ccaccaccat	caacctcttc	aaaacctact	ccctccctct	aagtatctct		60
caacacagta	tgtctggggc	tagatttcaa	aaccacgta	atgaaaaagt	cagttttaca		120
agcctaattt	tgttgttttt	ttttttatat	caattaacgt	taaaaattgc	atcaactatt		180
taattcatga	ggatctttca	tattaaaatt	taaccttaag	attcaaccgc	catgtgcttt		240
tataaaggaa	acatttttta	gagacgtctg	agctcacttt	tacatggtgg	tgccactatgc		300
cgttaatqtt	tqtqatttt						319

```
<210> 340
<211> 278
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(278)
<223> n = A,T,C or G
```

PCT/US99/30909

<400> 340

<210> 341

<211> 400

<212> DNA

<213> Homo sapien

<400> 341

<210> 342

<211> 536

<212> DNA

<213> Homo sapien

<400> 342

<210> 343

<211> 646

<212> DNA

<213> Homo sapien

<400> 343

aaaacttcta	tctatcaaaa	gacataaaga	aaacagtc	gccacagact	agggtgaata	60
tctcaataca	tatatccgac	aagagaattg	catctagaat	gtataaagaa	tttctatgac	120
ccaattatag	ctatcaggga	tatacaaat	aaaaccaaaa	tgaaacatca	ctacacaccg	180
attggaatgg	ttaaaaagga	aaaatactga	caacaccaat	atttgtaaag	acaggaggta	240
ccagaactct	cattcattat	attcataaat	tgacaaatat	aaaaactgct	atagtagggc	300
agtcttcctt	agaaagggat	tgtgggcatg	acagagaaca	atattaatct	gtccattata	360
ttccttaact	gtaaaatgga	gaccatatgt	tccaccagct	tcacttggtg	attatgatac	420
atggctatta	agagactcaa	atgactccat	ttcatcaact	aatatgccct	gtcaattcta	480
cttctaaga	atcccattgt	ctatccaatg	tcataccact	atcataattt	aagtgttcat	540
aactcttat	aatatttcaa	taatctaact	gggtctcaatg	cctgtagtag	aaattgcaga	600
ttgggctccc	caattttctgt	tccttaggaa	ggctgagaaa	gctttt		646

WO 00/37643

PCT/US99/30909

105

<210> 344
<211> 383
<212> DNA
<213> Homo sapien

<400> 344
cctgcacccc agtataaggg cctccccagc tgagtaagaa gctgcttccc ctctctcat 60
aggccaagcc tattgtgtga aaccatctca tggctctggg gacgtagacc atttttgaaa 120
ccgtctcatg gtcttggtga cgtagaccgt ttgcttcttt aactccagcc gcggaatgac 180
attagtggaa ccgggctagg gaactgctgg aagttcagga tcccaccacc ttgaacacct 240
aggccagggg tccccaccat gtcccggtt tctttcttcg agagtataga accgttcatt 300
cttgctttgt gtccattcc atctcttgaa aaaatgtagt ctttgaatgt gtgaaaatct 360
agggacattc aatctagtct ttt 383

<210> 345
<211> 263
<212> DNA
<213> Homo sapien

<400> 345
cctccccttc ccttttgcgt gtgggaggag ctgctgtgct ccttggccgc ttactggaag 60
ggcgtttttc agagctgcag ggacaggggtg agcagctgaa gggctaggag ggaagccggc 120
ccccgctctg cagaagctgc atttcagctg aatctgtgtt tcagcctcag ttggttgac 180
cgttagcccc tctcctcccg gatggctcatg tttttgtcac attagagaat aaacagccac 240
acacacattt ttttttttcc ttt 263

<210> 346
<211> 132
<212> DNA
<213> Homo sapien

<400> 346
aaatccaaat acaaaaagcat agtctctgca agattttgtt ctttgaattt cttgatattg 60
taattgatta ttgataactg tcatcatgaa attatctctc aataataaga taaataaact 120
agcatatgaa tc 132

<210> 347
<211> 564
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(564)
<223> n = A,T,C or G

<400> 347
cctgggtatc cagggagggt ctgcagccct gctgaagggc cctaactaga gttctagagt 60
ttctgattct gtttctcagt agtcctttta gaggttgct atacttggtc tgcttcaagg 120
aggctgacct tctaattgat gaagaatggg atgcatttga tctcaagacc aaagacagat 180
gtcagtgggc tgctctggcc ctggtgtgca cggctgtggc agctgttgat gccagtgtcc 240
tctaactcat gctgtccttg tgattaaaca cctctatctc ccttgggaat aagcacatac 300
aggcttaagc tctaagatag ataggtgttt gtccttttac catcgagcta cttcccataa 360
taaccacttt gcatccaaca ctcttcccc acctccata cgcaagggga tgtggatact 420
tggcccaaag taactggtgg taggaatctt agaacaaga ccacttatac tgtctgtctg 480

PCT/US99/30909

aggnagaaga taacagcagc atctcgacca gcctctgcct taaaggaaat ctttattaat 540
cacgtatggt tcacaagata attc 564

```
<210> 348
<211> 321
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(321)
<223> n = A,T,C or G
```

<400> 348							
gcncatgaac	angggagcaac	ganaagagat	gtcgggctaa	gggcccgga	cgggcggcac		60
ccatcctgcn	acggaacacn	ttcgggttnt	ggttttgatt	ngttcacctc	tgtttatatg		120
canctatttg	ntcctcctcc	cccaccccag	ncgcgaactt	catgcttntc	ttccgcnctc		180
agccnccctg	cctctgtctc	gcggtgagtc	antgaccaacn	gnttcccctg	cangagccgc		240
cgggcgtgag	acnncgacc	tcnntgcata	caccaggccg	ggcccnngct	ggctccccc		300
gnggcctgtg	gaanagctg	q					321

```
<210> 349
<211> 255
<212> DNA
<213> Homo sapien
```

<400> 349						
ccatgacagt	gaaggggctg	ttaggaatat	caacaccacc	gaagcgaca	tagatcacat.	60
atgtgcccg	cttggcagct	gtgtagaaga	tgtcataggt	tccatcttca	ttctcaatga	120
catcggcctc	ggcctcagtg	ccatctgggg	tcagaaccgt	gcaggtcaat	ttacccttcc	180
cggcagtcct	ggcatcaacc	acaaagccta	cttcttcgcr	agttttcaca	gtggaggcga	240
ttccaggacc	cgtag					255

```
<210> 350
<211> 496
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(496)
<223> n = A,T,C or G
```

<400> 350						
gggcttattn	gctcacaaaa	tcattcnctt	ttggaactat	ggccaattga	agctacacac	60
tgaattttatt	aatacagcat	taagtttctt	tgtgtnaaaa	aatctttgtt	cncagtaata	120
aaaaaagata	aggcaagatg	cattaaacat	gaaaccttct	ggctcttttc	ctctgcgttt	180
ttacagagcc	actgatgact	atctgcaaca	aaagagttaa	gtttctgatt	ttccgtatca	240
agcatcttat	gcctttgctg	tggtagaagt	tctggccaag	cacctgaag	gacagatgct	300
ggtgatggnc	tttggcactt	atgctggcaa	actgagcttc	tttcccttga	gtacttttgn	360
aatgtataag	tagaagaagt	cacaagtata	ggatggtctg	gactacgccg	gccaccacag	420
caatgaggtc	aaagaagccc	tcaagnaga	agcgnccaga	tccagttgac	aagatacaaa	480
gcacgataga	ggccca					496

<210> 351

<211> 109
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(109)
<223> n = A,T,C or G

<400> 351
ccatagtga gacctgggaat gactgttact gcagcatctg ggctgccanc cacaggaag 60
ggccaagccc catgtagccc cagtcactct gccagcccc gctcctgg 109

<210> 352
<211> 384
<212> DNA
<213> Homo sapien

<400> 352
ccttcgagag tgacctggct gccaccagg accgtgtgga gcagattgcc gccatcgac 60
aggagctcaa tgagctggac tattratgact caccagtggt caacgcccgt tgccaaaaga 120
tctgtgacca gtgggacaat ctgggggccc taactcagaa gcgaaggga gctctggagc 180
ggaccgagaa actgctggag accattgacc agctgtactt ggagtatgcc aagcgggctg 240
cacccttcaa caactggatg gagggggcca tggaggacct gcaggacacc ttcattgtgc 300
acaccattga ggagatccag ggactgacca cagcccatga gcagttcaag gccaccctcc 360
ctgatgccga caaggagcgc ctgg 384

<210> 353
<211> 345
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(345)
<223> n = A,T,C or G

<400> 353
ccttggtcag gatgaagtng gctgacacac cttagcttgg ntttgcttat tcaaaagana 60
aaataactac acatggaaat gaaactagct gaagcctttt ctgtttttan caactgaaaa 120
ttgnacttgg ncacttttgt gctggaggag gccattttc tgcttggcag ggggcaggtg 180
tgtgccctcc cgtgactcc tgetgtgtcc tgagggtgat ttctgttgn ncacacaang 240
gccangntcc atttccctc ccttttcacc agngccacan cctnntctgg aaaaangacc 300
agnggtcccg gaggaacca tttngctct gcttggacag canag 345

<210> 354
<211> 712
<212> DNA
<213> Homo sapien

<400> 354
ccatctacaa tagcatcaat ggtgccatca cccagttctc ttgcaacatc tcccacctca 60
gcagcctgat cgtcagcta gaagagaagc agcagcagcc caccagggag ctctgcagg 120
acattgggga cacattgagc agggctgaaa gaatcaggat tcttgaacct tggatcacac 180
ctccagattt gcaagagaaa atccacattt ttgccccaaa atgtctatct ttgacggaga 240

```

gtctaaagca gttcacagaa aaaatgcagt cagatatgga gaaaatccaa gaattaagag    300
aggctcagtt atactcagtg gacgtgactc tggaccaga caggcctac cccagcctga    360
tcctctctga taatctgcgg caagtgcggt acagttancc ccaacaggac ctgcctgaca    420
accccgagag gttcaatctg ttccctgtg tcttgggctc tccatgcttc atcgccggga    480
gacattattg ggaggtagag gtgggagata aagccaagtg gaccataggt gtctgtgaag    540
actcagtggt cagaaaaggt ggagtaacct cagcccccca gaatggaltc tgggcagtggt    600
ctttgtggta tgggaaagaa tattgggctc ttacctccca atgactgcc taccctgcg    660
gaccccgctc cagcgggtgg gggattttct tggactatga tgctggggga gg          712

```

<210> 355

<211> 385

<212> DNA

<213> Homo sapien

<400> 355

```

cctcatagcc gcttagcaca gttacagaat gtctgaaggg gacagtgtgg gagaatccgt    60
ccatgggaaa ccttcgggtg tgtacagatt tttcacaaga cttggacaga tttatcagtc    120
ctggctagac aagtcacac cctacacggc tgtgcgatgg gtcgtgacac tgggcctgag    180
ctttgtctac atgattcgag tttacctgct gcagggttgg tacattgtga cctatgcctt    240
ggggatctac catctaaatc ttttcatagc ttttctttct cccaaagtgg atccttcctt    300
aatggaagac tcagatgacg gtccttcgct acccaccaaa cagaacgagg aattccgccc    360
cttcattcga aggctccag agttt          385

```

<210> 356

<211> 347

<212> DNA

<213> Homo sapien

<400> 356

```

aaatgagata aagaaagtct ccttttgttt ttagatggaa aagaaagcac aagttttctc    60
tacctgtgaa tgaactttgg tgacctatat gtgccattca tgcagcattt ttgttcatat    120
tggcttagaa ttcagtgcac gaatatcatt acattcttat atctaacatt cctagttagc    180
tttgattcaa aatatacaaa atctgataca tgaatacttt gctagattaa tgacttgatc    240
atctttggaa tgagtaggca agacgatttt tacctattat ttctatgttg tgggtaatgt    300
taaaactaaa tacagatgat aataattgct atttcacagt gatgttt          347

```

<210> 357

<211> 313

<212> DNA

<213> Homo sapien

<400> 357

```

aaagtaatca acctctctgt ccttccatta gtctggatcg tctaaagatt gttttatttt    60
tagaggctca tccggtcaga tgtagtgat gtgaaatttc aggccaggcg tgacgtcagc    120
gtggcatttg aaacagctcc atgttgccct tagtgctgtc tgaccgaagc ctgtctgtcc    180
tcagatataa agatgaagcg cagctgtata aagaagagca cctgaggaat cggcagcacc    240
ctcactgcta cgttcagtac atgatcgcca tcatcaacaa ctgccagacc ttcaaggaat    300
ccatagtcag ttt          313

```

<210> 358

<211> 403

<212> DNA

<213> Homo sapien

<400> 358

WO 00/37643

PCT/US99/30909

109

```

aaaaagaagg acttaggggtg tcgttttcac atatgacaat gttgcattta tgatgcagtt      60
tcaagtacca aaacgttgaa ttgatgatgc agttttcata tatcgagatg ttcgctcgtg      120
cagtactggt ggttaaata gaattttatgt ggatttttga tgaatacac agtgagacac      180
agtaatttta tctaaattac agtgcagttt agttaatcta ttaatactga ctcaagtgtct      240
gcctttaaat ataaatgata tgttgaaaac ttaaggaagc aaatgctaca tatatgcaat      300
ataaaatagt aatgtgatgc tgatgctgtt aaccaaaggg cagaataaat aagcaaaatg      360
ccaaaagggg tcttaattga aatgaaaatt taattttgtt ttt                               403

```

<210> 359

<211> 411

<212> DNA

<213> Homo sapien

<400> 359

```

aaataaatac ttagaacacg acttggtctc tacaagcatc tggactctag gtctcagtac      60
tggagtgtct caccatggg cccacgcag ggacgccacg gtccctccc acccctgat      120
caagacacgg aatcggtgc cgatggttgg atcgcaatgc gcccttttc tagagccttc      180
cccgccatc tacaggcagg atgcgggtgg gaaaaagaca actggaattt ctcgaagggt      240
gatggteccg acggttgagg attctacgtg gttctcttgg ttcccttgt gtgtgtgtgt      300
gtggaggagg ccgcggccct tagatcacct tcttgagctc gtcgtacagg accagcacga      360
aggcgcccc catgccccgc aggaaggttg accacgcacc cttgaagaag g                               411

```

<210> 360

<211> 378

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(378)

<223> n = A,T,C or G

<400> 360

```

cctcttcagg ggcccgagcc agggacaggg ccttggtttc cttctccctg gcttctgct      60
cagctctgtc cctctcatcc gcgtatttgg aagagatgtt tttctcctcg gctaacaact      120
gatcaaatct cctctgcttc tttccaggt tggacacgag ttgccgctgg ttgtccaaat      180
180caacaaccag gtcgtccagc tctgtctgaa gcctgttctt ggtcttttcc agtttatcat      240
aagcggccgc cttctcctcg tactgctggg tgaggntctc gatctccttc tggaacctct      300
tcttcccttc ttccagagct tccacgngc tggcaaagtc ctgcagcttc ttcttcgagt      360
cgagagctg gatgttga                               378

```

<210> 361

<211> 372

<212> DNA

<213> Homo sapien

<400> 361

```

aaatactggg ggccattaag agtggatgta gctaagagct tagctaacat tgccttttca      60
ctctattttt ctcatagatt gtaagcattc tgtttttcaa tattgtagtt aattttttgg      120
ctttcaacag cagccctagt aatgggtggag ttgttaatta atgtgtatat tgtactgaat      180
ttctgtcagt taaggggttc actgctttgg tggaaattgg tggaaattgc tagcaggttc      240
cacgatgttt atttttttct ccatgttgta tatcattacc atttcacata cgcgtttcta      300
tttttcttcc tctcctcctg atctccttaa aaatgaatct agagttgggtg gctttttccc      360
cctcctcttt gg                               372

```

<210> 362
<211> 544
<212> DNA
<213> Homo sapien

<400> 362
cctgagtcac ctacataggt gttgcagcaa gccctggatt cagagtgtta aacagaggct 60
tgccctcttc aggacaacag ttccaattcc aaggagccta cctgagggtc ctactctcac 120
tggtgtcccc aggatgaaaa cgacaatgtg ccttttttatt attatttatt tgggtgtcct 180
gtgttattta agagatcaaa tgtataacca cctagctctt ttcacctgac ttagtaataa 240
ctcactactaa ctggttttga tgccctgggt gtgacttcta ctgaccgcta gataaacgtg 300
tgccctgtccc ccagggtggtg ggaataattt acaatctgtc caaccagaaa agaattgtgtg 360
tggttgagca gcattgacac atatctactt tgataagaga cttcctgatt ctctagggtc 420
gttcgtggtt atccccattgt ggaaattcat cttgaatccc attgtcctat agtcctagca 480
ataagagaaa tttcctcaag tttccatgtg cggttctcct agctgcagca atactttgac 540
atct 544

<210> 363
<211> 328
<212> DNA
<213> Homo sapien

<400> 363
aaactgggtt tgacaaaagc ctttagttgt gtttcttgaa ctataaagaa aacaaatttt 60
ggcagtcctt aagtatatat agcttaaaat ataattttta gcattttgca ccatatgtat 120
gccattatat ttgattttgc attactgttt cacaatgaag ctttctttaa ggctttgatt 180
tttatgatta tgaaagaaat aaggcacaac cacagttttt ctttcttaaa tttcatcact 240
gttgatgtgg ttctttttgtg ttaaaaaaaa aaagtgcac tatcaaaact aaaaaattat 300
agagtaatat tgccgttctg ctgatttt 328

<210> 364
<211> 569
<212> DNA
<213> Homo sapien

<400> 364
cctgggcacc tctttgcttg aaatatggca agacttgga aaatgtttgc ccttagaatc 60
tatctcacta ctttagttag ttgtctcctt tgggcctggg cacagttctg gccctgatct 120
ggaacagact cccttttcta aaactgaact tgaccacatc aaaagtgtgt aaaacaatct 180
ccatggtaat taaacttgca ttcaacacca tatggtaaca gaagatggca aaggataaga 240
ttcagatctt agatctttcc aagtagggca tgttagatga tagaaggatt agttgcaagc 300
tggatctgag ctccaggcttg ggcattgaag aaactgtctc ccatgtggtt tgggaagagt 360
aggggtctcc tgagctctat tgtgaactat acgggtttca tccaaggaaat ggtatgatgt 420
gggcataaaa ccattcttca gacaactgaa gatgggtccc ttctgtagcc agaaacacta 480
gctgtcctgc attgtccatt tcccttagcc ccaggcggtc ctgtgtgtac agggaggtct 540
ectgtaaggg aatgggttcc ttggcttgg 569

<210> 365
<211> 151
<212> DNA
<213> Homo sapien

<400> 365
aaaaaaaaa atccttttat tatggaattt gtcaaacaca cacacaagca taacaaacct 60

PCT/US99/30909

```
ctaggtagcc atctccaagt tttagccctt attataaatt catcttcagt gttttattat    120
ccacttcttc tctctctatc tttagtattt t                                     151
```

<213> Homo sapien

<223> n = A,T,C or G

agtataaaga	tatatcccat	aaaagagttt	ggcagtcaaa	ganaagcatc	gcacttccga	60
aaaacacaag	cattcttctc	ctagttctaca	gagaattgng	taaaaaaaaa	aaaaaatcat	120
catcaacagc	cncantnta	cncacacta	gaggttcac	tccggcaagt	aaattaaggn	180
tgcagtcctat	ccctgaacga	tganaagnng	tctgagctat	gycaaagngt	tanaaagtag	240
cccagctana	caaatgcccc	agctatcccc	aggggagtta	ttcagtaact	aanacttcat	300
ttccaananc	agccccggaa	aagccctgac	aggaaggggg	gaccagngat	caccgatntc	360
ccattagggg	cggnccacca	aaacaaatg	cctggagctt	ntgagcagct	gcagcctggg	420
gttgtggcta	ggcncngggn	ngngttgcaa	aaaaacggct	gtntccgggg	agaggcfaat	480
ggcaggccag	ccagccctgg	gtacatgg				508

<213> Homo sapien

cctgagcggc	tagtctttaa	gatgcgcttc	tatcgtttgc	tgcaaatccg	agcagaagcc	60
ctcctggcgg	caggcagcca	tctgatcatt	ctgggtgacn	tgaatacagc	caaccgcccc	120
attgaccact	gggatgcagt	caacctggaa	tgctttgaag	aggacccagg	gcgcaagtgg	180
atggacagct	tgctcagtaa	cttgggggtgc	cagtcctgct	ctcatgtagg	gcccttcctc	240
gatagctacc	gctgctttca	accaaagcag	gagggggcct	tcacctgctg	gtcagcagtc	300
actggcgccc	gccatctcaa	ctatggctcc	cggcttgact	atgtgctggg	ggacaggacc	360
ctggtcatag	gcacctttca	gg				382

<213> Homo sapien

ccttctccct	ccttgacaag	gatggagatg	gcactatcac	caccaaggag	ttggggacag	60
tgatgagatc	cctgggacag	aaccccactg	aagcagagct	gcaggatatg	atcaatgagg	120
tggatgcaga	tgggaacggg	accattgact	tcccggaagt	cctgaccatg	atgg	174

<213> Homo sapien

aaatctcatg ggttctatta aaaaaatata tatatagggc cccaatccat tgccatcaaa 60

PCT/US99/30909

ttgcccttgg	acttttccaa	ggatatattat	gggggttttat	gcaaaattcc	aagctaccat	120
gtaacttttt	ttaaccattt	aacaaggagg	gggaactgtt	tcttaccctc	tttacatgtt	180
gtgcattgtt	gtggtccaga	aatgccaaac	cttttt			216

<400> 370

ccttggtcag	gatgaagttg	gctgacacag	cttagcttgg	ttttgcttat	tcaaaagaga	60
aaataactac	acatggaaat	gaaactagct	gaagcctttt	cttgttttag	caactgaaaa	120
ttgtactctg	tcactttttg	gcttgaggag	gcccattttc	tgcttggcag	ggggcagggtc	180
tgtgcccttc	cgctgactcc	tgtctgtctc	tgaggtgcat	tccctgttgt	acacacaagg	240
gccaggctcc	attctctctc	cttttcacc	agtgccacag	ctctgtctgg	aaaaaggacc	300
aggggtcccg	gaggaaccca	tttgtgctct	gcttggacag	cagg		344

<220>

```
<221> misc_feature
<222> (1)...(741)
<223> n = A,T,C or G
```

<400> 371

aaattacata	tctaatttgg	tgatttggtta	aatgccatt	tcttcattcta	agtgtcaagt	60
gctaagt:gt	gcagtttgg	ccttgctaca	ctccaaggca	caaaggagtt	caagggaatgt	120
gcaatggaaa	tcagtttagat	gaatgtgtta	ggaaccttcc	ctttaataaaa	gctggatccc	180
acactagccc	ctacacccct	tcatacccaa	atattcctgc	tctctctcac	ctgcacttgc	240
tgtctctctc	tgtgccacac	aaatctacct	ctcaagccta	ggtcccacct	gcttcatgac	300
aacctttccag	actattccag	aaaccttaac	catctctgac	ctctcatcag	atctatgttg	360
tacataacac	caattaatga	gatacttact	gctttatgct	ctaattgctt	cctgtattca	420
aaatcttctc	tccaaccaca	taatgactcc	ctaaacttct	cttgattttt	ccaatgcctt	480
gtacaagcac	agaactggtc	aatcaataaa	tactcactgg	ttatttgagg	aaaaaatggt	540
gccaagcacc	atctttatca	gaaaataaat	caattcttct	aaacttggag	aaatcaccct	600
attcctagta	tgtgatctta	attagaacaa	ttcagattga	gaangngaca	gcattgctggc	660
agtctctcaga	gcctctgctt	gctctcggna	cctcctgc	tgggtcccca	ctttgggtggc	720
at ttgaggag	cccttcagcc	t				741

<220>

```
<221> misc_feature
<222> (1)...(218)
<223> n = A,T,C or G
```

<400> 372

ccgccagtgt gctggaattc gcccttggcc gcccgggcag gtaccacaac agcaggnctg 60

```

agtgagaaat ctaccacctt ctacagtagc cccagatcac cggacacaac actctcacct    120
gccagcacga caagctcagg cgtcagtga  gaatccacca cctccacag cgcaccaggc    180
tcaacgcaca caacagcatt ccctggcagt accttggg    218

```

```

<210> 373
<211> 168
<212> DNA
<213> Homo sapien

```

```

<400> 373
actgctaggg aatgctgttg tgtgcattga gcctgggctgg ctgtgggagg tgggtggattc    60
ttcactgacg cctgagcttg tctgtctggc aggtgagag* gttgtgtccg gtgatctggg    120
gctactgtag aagggtgtag atttctcact caggcctgct gttgtggg    168

```

```

<210> 374
<211> 154
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(154)
<223> n = A,T,C or G

```

```

<400> 374
tgagaaatct accaccttct acagngagcc ccanatcacc ggacacaaca ctctcacctg    60
ccagcacgac aagctcaggc gtcagtgaag aatccaccac ctccacagc cgaccaggct    120
caacgcacac aacagcattc cctggcagta cctc    154

```

```

<210> 375
<211> 275
<212> DNA
<213> Homo sapien

```

```

<400> 375
actgccaggg gacagtgctg tgtcagttga acctgggctg ctgtgggaag ttgttgattc    60
ctgactgggg cctgaggttg tgggtctggc aggtaacagt gttgtatccg ttgagcctgg    120
gctgctgtgg gaagtgttag aatgccgact gaggcctggc gtggtggtgc tgcaggggaa    180
tgctgttggt tgcgttgagc ctggtcggct gtgggaggtg gtggattctt cactgacgcc    240
tgagcttgtc gtgctggcag gtgagagtgt tgtgg    275

```

```

<210> 376
<211> 191
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(191)
<223> n = A,T,C or G

```

```

<400> 376
actgccaggg gacagtgctg tgtcagttga acctgagctg ctgtgggaag ttgttgattc    60
ctgactggag cctgaggttg tgggtctggc aggtaacagt gttgtatccg ttgagcctgg    120
gctgctgtgg gaagtgttag aatgccgact gaggcctggc gtggtggtgc tgntagggaa    180

```

tgctgctagc g

191

<210> 377
 <211> 476
 <212> DNA
 <213> Homo sapien

<400> 377

ccgccagtgt gctggaattc gcccttggcc gcccgggcag gtacatttcc ttgtagactc	60
tgtaatttc ctgcagctcc tgggtgggtc tggagcagat gatctcaatg agagagtcct	120
cgtcgggtcc cagcccttc atggaagctt ttagctcaga agcgtcatac tgagcagggtg	180
tcttcaatag gcccaaatc accgtctcca ggtggccaga tgggctgac ttcagtgtg	240
atgcaagttc ctttttggtc cttctctggt aggcgaaggc aatatcctgt ctctgtgcat	300
tgctgcggtt ggtcaaatg ttgacaatgg tgacctcatc cacacctttg gtcttgatgg	360
ctgtttcaat gttcaagca tcccgtctcag catcaaagtt agtataggct ttgacagacc	420
catatgcact tgggggtgta gattgatcac cctccaagcc yagcttgac aggatt	476

<210> 378
 <211> 455
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(455)
 <223> n = A,T,C or G

<400> 378

agtgtgctgg aattcgccct tggccgccc ggcaggtaca catcccatct tcaaatttaa	60
aatcatattg tcagttgtcc aaagcagctt gaatttaaaag tttgtgctat aaaattgtgc	120
aaatatgtta aggatgaga ccaccaatg cactactgta atatttcgct tccataattt	180
cttcaccta cagataatag acaacaagtc tgagaaacta aggctaacca aacttagata	240
taaatctac caataaaatt tttcagtttt aagttttaca gtttgattta aaaacaaaac	300
agaaacaaat ttcaaaataa atcacatctt ctcttaaaac ttggcaaac cttccctaac	360
tgtccaagtn tgagcataca ctgccactgg ctttagatac tccaattaaa tgcactactc	420
tttactgggt ctgaatgaag tatggtgaaa caagc	455

<210> 379
 <211> 297
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature
 <222> (1)...(297)
 <223> n = A,T,C or G

<400> 379

agctcggatc cctagnacgg ccgccagtgt gctggaattc gcccttagcg gcggcccg	60
caggtacaaa gaatccttag acgccatact gagttttaag ttccttaatt cctaatttaa	120
ggcttctagt gaagcctcct cacagtaggc ttcactaggc ccacagtgcc cctagacctc	180
tgacaatccc accctagaca gactttattg caaaatgcgc ctgaagaggc agatgattcc	240
caagagaact caccaaatca agacaaatgt cctagatctc tagtgtgna gaactat	297

<210> 380

PCT/US99/30909

```
<211> 144
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(144)
<223> n = A,T,C or G
```

```

<400> 380
actttgctga aaattctttt tcccagggtc tataaaacat taatttgttt ttatatttta 60
ctattttttt gngttttttt gtttttaaat caataagtaa tctaggacta gcattatggt 120
tgctagacct ggcatttgct cggc                                     144

```

```
<210> 381
<211> 424
<212> DNA
<213> Hcmo sapien
```

<400> 381						
actcttgaat	acaagtttct	gataccactg	cactgtctga	gaatttccaa	aactttaatg	60
aactaactga	cagcttcatg	aaactgtcca	ccaagatcaa	gcagagaaaa	taatttaattt	120
catgggacta	aatgaactaa	tgaggataat	attttcataa	ttttttattt	gaaatttttgc	180
tgattcttta	aatgtcttgt	ttcccagatt	tcaggaaact	ttttttcttt	taagctatcc	240
acagcttaca	gcaatttgat	aaaacatact	tttgtgaaca	aaaattgaga	cattthacatt	300
ttctccctat	gtggctgctc	cagacttggg	aaactattca	tgaattattta	tattgtatcg	360
taatatagtt	attgcacaag	ttcaataaaa	atctgctctt	tgtataacag	aatacatttg	420
aaaa						424

```
<210> 382
<211> 408
<212> DNA
<213> Homo sapien
```

<400> 382							
actcttgaat	acaagtttct	gataccactg	cactgtctga	gaatttccaa	aactttaatg		60
aactaactga	cagcttcacg	aaactgtcca	ccaagatcaa	gcagagaaaa	taattaattt		120
catgggacta	aatgaactaa	tgaggataat	atthtcataa	ttttttattt	gaaattttgc		180
tgattcttta	aatgtcttgt	ttcccagatt	tcaggaaact	ttttttcttt	taagctatcc		240
acagctttaca	gcaatttgat	aaaataatac	tttgtgaaca	aaaattgaga	catttacatt		300
ttctccctat	gttgcgcgtc	cagactttggg	aaactattca	tgaattattta	tattgtatgg		360
taataatagtt	attgcacaag	ttcaataaaa	atctgctctt	tgtagtac			408

```
<210> 383
<211> 455
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(455)
<223> n = A,T,C or G
```

<400> 383
actcttgaat acaagtttct gataccactg cactgtctga gaatttccaa aactttaatg 60

PCT/US99/30909

aactaactgn	cnncttcattg	aaactgtcca	ccaagatcaa	gcagagaaaa	taattaattt	120
catgggacta	aatgaactaa	tgaggataat	attttcataa	ttttttattt	gaaattttgc	180
tganncttta	aatgtcttgt	ttcccagatt	tcaggaaact	ttttttcttt	taagctatcc	240
acagcttata	gcaatttgat	aaaatatact	tttgtgaaca	aaaattgaga	catttacatt	300
ttctccctat	gtgggtcgctc	cagacttggn	aaactattca	tgaatattta	tattgtatgg	360
ttaatatagtt	attgcacaag	ttcaataaaa	atctgctctt	tgtataacag	aatacatttg	420
aaaacattgg	ttattattacc	aaqactttga	ctaga			455

<213> Homo sapien

<223> n = A, T, C or G

actttgaat	acaaggttct	gatatcactg	cactgtctga	gaatttcaa	aactttaatg	60
aactaactga	cagcttcctg	aaactgtcca	ccaagatcaa	gcagagaaaa	taattaattt	120
catgggacta	aatgaactaa	tgaggataat	attttcataa	ttttttattt	gaaattttgc	180
tgattcttta	aatgtcttgt	ttcccagatt	tcaggaaact	tttttttttt	tcaagctatc	240
cacagcttac	tgcaatttga	taaaatatac	ttttgngaac	aaaaattgag	acattttacat	300
ttttctccca	agtgggcgct	ccagacttgg	gaaactattc	atgaatatatt	atat.tgnatg	360
ggaatatagc	attgcc					376

<213> Homo sapien

acctgtgggt	ttattacctt	tgggtttata	tcttcaaata	cgacattcta	gtcaaagtct	60
tggtaatata	accaatgttt	tcaaatgtat	tctgtcatat	aaagagcaga	tttttattga	120
acttgtgcaa	taactatatt	accatacaat	ataaatattc	atgaatagtt	tcccaagtct	180
ggagcgacca	catagggaga	aaatgtaaat	gtctcaattt	ttgttcacaa	aagtatat	240
tatcaaattg	ctgtaagctg	tggatagctt	aaaagaaaaa	aagtttcctg	aaatctggga	300
aacaagacat	ttaaagaatc	agcaaaattt	caataaaaaa	attatgaaaa	tattatcctc	360
attaagttcat	ttagtcccat	gaaattaatt	atcttctctg	cttgatcttg	gtggacagtt	420
tc						422

<213> Homo sapien

caagtaggtc	tacaagacgc	tacttccct	atcatagaag	agcttatcac	ctttcatgat	60
cacgccctca	taatcatttt	ccttatctgc	ttcctagtc	tgtatgccct	tttcctaaca	120
ctcacaaaca	aactaactaa	tactaacatc	tcagacgctc	aggaaataga	aaccgctcga	180
actatctctgc	ccgccatcat	cctagtcctc	atcgccctcc	catccctacg	catcctttac	240
ataacagacg	aggtcaacga	tccctccctt	accatcaaat	caattggcca	ccaatggtac	300
tgaacctacg	agt					313

<210> 387
<211> 236
<212> DNA
<213> Homo sapien

<400> 387
cgccctcata atcattttcc ttatctgctt cctagtcctg tatgcccttt tcctaacact 60
cacaacaaaa ctaactaata ctaacatctc agacgctcag gaaatagaaa ccgtctgaac 120
tatectgccc gccatcatcc tagtctcat cgccctccca tccctacgca tcctttacat 180
aacagacgag gtcaacgata cctcccttac catcaaatca attggccacc aatggg 236

<210> 388
<211> 195
<212> DNA
<213> Homo sapien

<400> 388
acgccctttt cctaacactc acaacaaaac taactaatac taacatctca gacgctcagg 60
aaatagaaac cgtctgaact atcctgcccg ccatcatcct agtctctatc gccctcccat 120
ccctacgcat cctttacata acagacgagg tcaacgatcc ctcccttacc atcaaatcaa 180
ttggccacca atggg 195

<210> 389
<211> 183
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(183)
<223> n = A,T,C or G

<400> 389
taacactcac aacaaaacta actaatacta nnatctcaga cgctcaggaa atagaaaccn 60
cctgaactat cctgcccgcg atcatcctag tcctcatcgc cctcccatcc ctacncatcc 120
tttacataac agacgagggtc aacgatccct cccttaccat caaatcaatt ggccaccaat 180
ggt 183

<210> 390
<211> 473
<212> DNA
<213> Homo sapien

<400> 390
acaaagcagc aactgcaata ctcaagggtta aaacattaga aaagcatttg tgtgacagg 60
atattacagt attatcaaaa tattacattt tcagacttac ttagcagata atcatccacc 120
agagcttaaa cttttaaatt atttccatag tcttaaaaaa tatgtaatgt cagaatgcat 180
ataaaaagaa tgtaaaagga aacctaataa acaaatggaa taatgtaaca aataaatatt 240
tgatttcagt aactgttaat aatcagctca acaccaccat tctctctaaa ctcaatttaa 300
ttcttatagg aataatgaac tgtcaaatgc catggcataa ttatttattt ccaagctatc 360
atcaatgatt agaactaaaa aaaatttggc ataaaaaat cacaattcag cataaataaa 420
gctattttta gcttcaacac tagctagcat ctctaagaat tggtgaaata agt 473

<210> 391
<211> 216

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 391

atttgatatt	taggtttcct	tttacattct	ttttatatgc	nntctgacat	tacatatatt	60
ttaagactat	ggaaataatt	taaagattta	agctctgggtg	gatgattatc	tgctaagtaa	120
gtctgaaaat	gtaatatatt	gataatactg	taatatacct	gtcacacaaa	tgcttttcta	180
atgttttaac	cttgagtatt	gcagttgctg	ctttgt			216

<210> 392

<211> 98

<212> DNA

<213> Homo sapien

<400> 392

acttattttca	acaattctta	gagatgctag	ctagtgttga	agctaaaaat	agctttattt	60
atgctgaatt	gtgatttttt	tatgccaaat	ttttttta			98

<210> 393

<211> 397

<212> DNA

<213> Homo sapien

<400> 393

tgccgatata	ctctagatga	agttttacat	tggttgagcta	ttgctgttct	cttggggaact	60
gaactcactt	tctctctgag	gctttggatt	tgacattgca	tttgaccttt	tatgtagtaa	120
ttgacatgtg	ccagggcaat	gatgaatgag	aattctacccc	cagatccaag	catcctgagc	180
aactcttgat	tatccatatt	gagtcaaatg	gtaggcattt	cctatcacct	gtttccattc	240
aacaagagca	ctacattcat	ttagctaaac	ggattccaaa	gagtagaatt	gcattgaccg	300
cgactaattt	caaaatgctt	tttattatta	ttatttttta	gacagtctca	ctttgtcgcc	360
caggccggag	tgcagtggtg	cgatctcaga	tcagtggt			397

<210> 394

<211> 373

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(373)

<223> n = A,T,C or G

<400> 394

ttacattggt	gagctattgc	tggtctcttg	ggaactgaac	tcactttcct	cctgaggctt	60
tggatttgac	attgcatttg	accttttatg	tagtaattga	catgtgccag	ggcaatgatg	120
aatgagaatc	tacccccaga	tccaagcatc	ctgagcaact	cttgattatc	catattgagt	180
caaatggtag	gcatttccta	tcacctgttt	ccattcaaca	agagcactac	attcatttag	240
ctaaacggat	tccaagaggt	agaattgcat	tgaccacgac	tantttcaaa	atgcttttta	300
ttattattat	tttttagaca	gtctcacttt	gtcgcccagg	ccggagtgca	gtggtgcat	360
ctcagatcag	tgt					373

PCT/US99/30909

```
<210> 395
<211> 411
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(411)
<223> n = A,T,C or G
```

<400> 395						
actgatcatt	ctattttccc	ctctattgat	ccccacctcc	aaatatctca	tcaacaaccg	60
actaatcacc	acccaacaat	gactaatcaa	actaacctca	aaacaaatga	taaccataca	120
caacactaaa	ggacgaacct	gactctttat	actagtatcc	ttaatcattt	ttattgccac	180
aactaacctc	ctcggactcc	tgcctcactc	atttacaccc	accacccaat	tatctataaa	240
cctagccatg	gccatcccc	tatgacggcg	cgcagtgatt	ataggctttc	gctctaagat	300
taaaaattgc	ctagcccaat	tcttaacngc	aggcacacct	acacccctta	tcccataact	360
agttattatc	gaaaccatra	gcctactcat	tcaaccaata	gccttgcccg	t	411

```
<210> 396
<211> 411
<212> DNA
<213> Homo sapien
```

<400> 396							
actgatcatt	ctatttcccc	ctctattgat	ccccacctcc	aaatatctca	tcaacaaccg		60
actaattacc	acccaacaat	gactaatcaa	actaacctca	aaacaaatga	tagccataca		120
caacactaaa	ggacgaacct	gatctcttat	actagtatcc	ttaatcattt	ttattgccac		180
aactaacctc	ctcggaactcc	tgcctcactc	atttacacca	accacccaac	tatctataaa		240
cctagccatg	gccatccctt	tatgagcggg	cgcagtgatt	ataggccttc	gctctaagat		300
taaaaatgcc	ctagcccact	tcttaccaca	aggcacacct	acacccttta	tcccataact		360
agttattatc	gaaaccatca	gcctactcat	tcaaccaata	gccttgcccg	t		411

```
<210> 397
<211> 351
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(351)
<223> n = A,T,C or G
```

<400> 397						
ngccgangta	caaaaaaaaaag	cacattccta	gaaaaaaggta	ttggcaaata	gtaaaaatgg	60
gagggtcaaaa	ncaaaaaaaaa	aaaaaacaaa	acnaaaaaaa	gaaaaaacca	acaattcttc	120
aattcagtg	gcaaacatta	tataaaaaa	gaaatactaa	ctctacagg	agtatttct	180
gataaaatt	ttaaattagca	tatctacnca	atctgagata	tctattccca	tggcaatgag	240
aaaaataattt	ataaaaaataa	agcaattgta	taccanatga	tagaaaaaaa	cataactttc	300
aaaaattqta	tttaacattt	caatgctatt	tccttattgn	gaatncttct	c	351

<210>	398
<211>	363
<212>	DNA

<213> Homo sapien

<400> 398

acaaaaaaaa	gcacattcct	agaaaaaggt	attggcaaat	agtaaaaatg	ggagggtcaaa	60
agcaaaaaaa	aaaaaaaaaa	aacaaaaaaa	agaaaaaacc	aacaattctt	caattcagtg	120
tgcaaacatt	atataaaaa	agaaatacta	actctacagg	cagtatttcc	tgataaatta	180
tttaaatagc	atatctacac	aatctgagat	atctattcca	atggcaatga	gaaaaaattt	240
tataaaaaa	aagcaatggt	ataccagatg	atagaaaaaa	acataacttt	cagaaattgt	300
atttaacatt	tcaatgctat	ttccttattg	ggaatacttc	tctgcagagt	ttttatgcta	360
tgt						363

<210> 399

<211> 360

<212> DNA

<213> Homo sapien

<400> 399

actgtttcct	cgtggttcag	gggtgtgcat	gaaggctctt	aggagagcaa	acacctgttc	60
ctattctgta	tgtccctccc	tcatttcaaa	tgagagtaac	caattgagta	aaataaccaa	120
ataaccattg	ccccaccatg	aacatggggc	ttgggaagac	agtcctacaa	tcttcatcat	180
atatttaggt	ttttaggcca	gccagctctt	tttttccaaa	gctttctttt	gaataaccgc	240
ccgggcggcc	cctaaggcg	aattctgcag	atatccatca	cactggcggc	cgctcgagca	300
tgcattctaga	gggcccaatt	cgccctatag	tgagtcgtat	tacaattcac	tggccgctgt	360

<210> 400

<211> 87

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(87)

<223> n = A,T,C or G

<400> 400

ctgcacatat	cnattacact	ggcggccgct	cgagcatgca	tgnagagggc	ccaattctcc	60
ctatattgag	tggaattaca	atnncnt				87

<210> 401

<211> 328

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(328)

<223> n = A,T,C or G

<400> 401

accaggggac	acaaacactc	tgcctaggaa	aaccagagac	ctttgttcac	ttgtttatct	60
gctgaccttc	cttcactat	tgtcctatga	ccttgccaaa	tccccctctg	cgagaaacac	120
ccaagaatga	tcaataaaaa	ataaaataaa	attaaattaa	aaaaaaaaaa	agagaggaac	180
ccacaaaaaa	aaaaaaaaag	aaagtntata	aaataaaata	ttgaagtcc	ttccatttaa	240
aaaaaaaaaa	aagaaaaagc	acggactctt	tcattccagt	ctgatgtgat	tatctctgga	300
aggcattttc	tcctctctct	ccctcccc				328

PCT/US99/30909

```
<210> 402
<211> 268
<212> DNA
<213> Homo sapien
```

```
<220>  
<221> misc_feature  
<222> (1)...(268)  
<223> n = A,T,C or G
```

<400> 402							
nacataatga	caacatcttc	actagactga	gtgttcaagg	atttgagatg	attcgctatt	60	
catcacacc	cgaagattga	gatccactgt	atttacacaa	agcaaagcca	tgtcagcaag	120	
ggactgtcaa	cctgattctg	agaacataaa	cattcaaaat	ttattttcca	gtgttccttt	180	
tgggaacca	acaacacatc	tttaatacct	acacacacac	acatctntac	ctttaaaaaa	240	
aaaaaaaaag	tgnaacttca	cagatagt				268	

```
<210> 403
<211> 538
<212> DNA
<213> Homo sapien
```

<400> 403						
acagtgatag	ctccccctgg	gcaatacaat	acaagaacag	tgggttttgt	caaat.tggaa	60
caaggaaaca	gaaccacaga	aataaataca	ttggttaaca	tcagattagt	tcaggttact	120
tttttgtaaa	agttaaagta	gaggggactt	ctgtattatg	ctaactcaag	tagactggaa	180
tctcctgtgt	tctttttttt	tttaaattgg	ttttaatttt	ttttaattgg	atctatcttc	240
ttccttaaca	tttcagttgg	agtatgtagc	atttagcacc	actggctcaa	tgcgctcacc	300
taggtgagag	tgtgaccaa	tcttaaagca	ttagtgctat	tatcagttac	caccatttgg	360
ggctttttatc	cttcattgggt	tatgatgttc	tctcatgtac	acatttctc	gagttttgta	420
attccagcca	aagagagacc	attcactatt	tgatggctgg	ctgcattcgag	acatttaaag	480
cttttagaga	atacactaca	ccagggagta	tgactactag	tatgactatt	aggaggggt	538

```
<210> 404
<211> 310
<212> DNA
<213> Homo sapien
```

<400> 404						
tttttttata	gatacaattg	ggtttttattt	gtgattcctg	agtcaggggca	gtttccattc	60
tgcaaaatat	agtgatagct	cctactgggc	aatacaacag	tagaacagtg	ggttttgtaa	120
aatgggaatc	caggaacaga	agaatataaa	taaattgatt	taaataaaact	gatttggttaa	180
tttcagaata	cttcatatta	cttttttcta	agagttaaaag	cagaaaggac	tttcttactg	240
tgctgactca	gacagcctgg	actctcatgt	ttttaggaaa	attttgtctg	ttctgggatac	300
tacctgcttc						310

```
<210> 405
<211> 559
<212> DNA
<213> Homo sapien
```

```

      <400> 405
acaatcaca attattaact cactggtagg gcagtgatga tcaaaccaat tgcattcatc      60
catgctgtaa tggtctctct tggcactaaa ggctgactgc agccggcaaa aaagaatgta     120

```

```

agtatgaatt tataaaaaca ttttagatgg ctgacaacgg atcttatttt taaagaatat 180
gtctaatcca gaggatcgac aactaatcca tttcaataaa acaatgggga attttttatt 240
gaataaaaaat gtaatatgca taaaaactca agaaggcttt ttaaaaatac ttccctcccca 300
atcattatcc catacttcat gctaattttt aaaagaatct tgaaatcttg aaaacaagat 360
gaagagaatc ttgttttaag tgacaagtta acattattcc tatattaaat gtcaaaactgc 420
tattaatgag tagaagtagg aacaaacccg gatcttagga tcctgtccag ggctcattcc 480
ataactccta tatcacaag acaagatctg gaaccagaaa acagtcacat tccaatgtgc 540
atcagccttg cggcaacag

```

<210> 406

<211> 427

<212> DNA

<213> Homo sapien

<400> 406

```

acaacagaat atctcgggaa tggactcaga agtatgccat gtgatgctac cttaaagtca 60
gaataacctg cattatagct ggaataaact tttaaatact gttccttttt tgattttctt 120
atccggctgc tcccctatca gacctcatct ttttttattt tattttttgt ttacctcctt 180
ccattcattc acatgctcat ctgagaagac ttaagttctt ccagcttttg acaataactg 240
cttttagaaa ctgtaaaagta gttacaagag aacagttgcc caagactcag aatttttaae 300
aaaaaaaaatg gagcatgtgt attatgtggc caatgtcttc actctaactt ggttatgaga 360
ctaaaacat tctcactgc tctaacatgc tgaagaaatc atctgagggg gagggagatg 420
gargctc

```

<210> 407

<211> 419

<212> DNA

<213> Homo sapien

<400> 407

```

acaatttgta gttgtttcca ggtttggcta ataatcattc cttaacctag aattcagatg 60
atcctggaat taaggcaggt cagaggactg taatgataga attaaattag tgtcactaaa 120
aactgtccca aagtgtgct tcttaatagg aattcattaa cctaaaacaa gatgttacta 180
ttatatcgat agactatgaa tgctatttct agaaaaagtc tagtgccaaa tttgtcttat 240
taaataaaaa caatgtagga gcagcttttc ttctagtttg atgtcattta agaattacta 300
acacagtggc agtggttaa atgaagtgctg tctacaaggc agataatata ctgtttgata 360
ctcaaaacat ttttcatttt gtttaaagta gaagttacat aattctatat tttaagtct 419

```

<210> 408

<211> 523

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1) ... (523)

<223> n = A,T,C or G

<400> 408

```

acatttgatg ttatgtgaat gttgagtttt tttcttctaa ttttcacttc agcagtgttt 60
agggctttca gatgccttat tccagtgtga acagaaaaag ttcatatttt atgtgggttaa 120
tgctttgatg tgtcacataa agagtgttt gttagaaaat ttggcacaat ttttaacttct 180
tagtggttg tgacattata tattatatat atatgtatat atatctttat aacattcctg 240
tgtttagtag tgtaaatgtt ctgggcaagt ttttaatatt tgaatgcctt tggatattcc 300
agcaataaag gcatcatgtt ctgcaatagg atttcttact catttaccta ttttaacact 360

```

aaaatagacc acaactgagc acaaattcct ttataaatg ttatagaagc agggaagaat 420
aataaacaca ttgtgaatt gtggttcagt ttatttatct ttagggaagg ctgatcattt 480
atcttatagc acataacccc agcctcttat tcattatggn taa 523

<210> 409

<211> 191

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(191)

<223> n = A,T,C or G

<400> 409

accccgtagt gatgagcact gactggttca ctggccacat tttagttctt cataataata 60
ggccacaaaa gggctctgtg gtttgccctc atgtgcactg gccctcccc acccctaggg 120
ggcactcagt agctgctgag aaggcctgtc caggangctg ttggaacccc ttcaataaat 180
acttagaagn a 191

<210> 410

<211> 403

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 410

acactggcca gtgtgttttt ggcgattaaa cataatcctg tgaatcagat taattcactt 60
gctgagtgtt catttgcggc atccctctgt tgggtcttgg gggccctcca cgacctctgt 120
gggctccccg tggctcactc tgccagagc ctgcttgaa attctgctga tatccatccc 180
gttgatagcc agagtaatcc cggggagcac tgaactgaga ctgtgtataa cactgtttg 240
gagtgttaga gaatgaaggc cggttaacct catatcctcc tctgaatcca ttggcagggc 300
cccggtatcc attcatcaag cctctagcac caggggagcc tccacgagac acaccacgac 360
tattgtaata gggctgattg ctacgtggaa atccagtgn tctg 403

<210> 411

<211> 384

<212> DNA

<213> Homo sapien

<400> 411

acgtgaaatc ataacaacat gttctcttgt gtttggtctc tcttgctcag catgatattt 60
ttacgggttca cccatattgc atgtatcagg aatataatcc tttttattat tgagtagtgt 120
tctattgtat gtatatacca cagtttattt ctcccttcat cctttgctag attttggggt 180
tttttcacat tgcgctattc aagtataaac ctgctctcaa cattcatgtg caagtctttg 240
agtggacata tatttgccgt ttctcttgag tgaatgcacc ttgttgggtc acgtggctta 300
atttaaaaaa attttaatca ctgtggtgca tatgtagtga ttattagtga ttatctcata 360
attttatttt cttgatgact aatg 384

<210> 412

<211> 315

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(315)

<223> n = A,T,C or G

<400> 412

acaatatttc	tcctttgaga	agataggata	tatgattttc	ccaaaaatca	caactttgaa	60
ggaagactta	nttctgact	tcaattatat	cctggaactg	gcaacttggt	cccttccttt	120
gcttcaaaaa	aagtgtgaga	aagagtgata	agatcaactt	taatcattct	tggatcttca	180
gcaaattcag	gatcaatgta	gaaaaacact	ggcatatct	cttcctcttg	gggattaagc	240
ctttgttctt	caaaacagaa	gcaactgtatt	ttattgaaat	actgtccacc	ttcaaatgga	300
acaatattgt	atgna					315

<210> 413

<211> 554

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(554)

<223> n = A,T,C or G

<400> 413

acaggtttca	ctattacaaa	tatatgatgt	taaactaaca	aactcatgac	cttcaaagat	60
gtcttcgtcc	cacgcacaca	catttgtaat	ttgtgtccat	ttgtatttcc	ccctcttcta	120
taatcttcaa	attatatagt	tatgcattga	gttccctatg	catctcacc	atctccttta	180
tctcagcctt	ctcatacttt	gccattctct	tctttctgga	aataaccagc	acaacaattc	240
cagcaacaac	tgctatcacc	acaaccacaa	taacagcaat	aacaccagct	tttagaccct	300
gcattgagaa	ttcaggtgct	ttttcatcaa	cataataaat	taaagtgtga	ccaggatcca	360
gatccagttg	ttccccattt	actgtcaggt	gccattttct	tagaatgaaa	caaggattca	420
cccttaacat	cttttttcaa	ataataagcc	acatcagcta	tgtccacatc	attctgagnt	480
ttttgagaag	aattttgaa	cagatcaata	gtgataacat	tattctcata	caaaatactc	540
gngataaatt	ntgg					554

<210> 414

<211> 267

<212> DNA

<213> Homo sapien

<400> 414

accagaaagg	cacacgattt	tacaatattt	gttggaatta	ccttactttt	taacctcctc	60
atagcagttt	tggtttgagt	atattgatga	aagccaaagt	ctggtatcta	aaacttgggc	120
caatgtttcc	caactgggat	atgtcaggct	ttcccaatag	cttaactgtg	accctatacg	180
gatggctttt	tagatagttc	tatactgctg	tattgtgtta	gcacttttct	ttgtcattaa	240
caacacactt	taaatagacat	ttggtga				267

<210> 415

<211> 454

<212> DNA

<213> Homo sapien

<400> 415

accggaacct	gcagaaacag	tgtgagaaat	taagtcctgg	ttcactgcgc	agtagcaaag	60
atgggtcaagg	ccatggaaaa	agcagaaatt	taccaagaaa	gctgataccc	atgtatagtt	120
cccactcatc	tcaaatacat	ctgctatctt	tttaagctaa	gtcctagaca	tatcggggat	180
aacatggggg	ttgattagtg	accacagtta	tcagaagcag	agaaatgtaa	ttccatattt	240
tatttgaaac	ttattccata	ttttaattgg	atattgagtg	attgggttat	caaacaccca	300
caaactttaa	ttttgttaaa	tttatatggc	tttgaaatag	aagtataagt	tgctaccatt	360
ttttgataac	attgaaagat	agtattttac	catctttaat	catcttgga	aatacaagtc	420
ctgtgaacaa	ccactctttc	acctagcagt	atga			454

<210> 416

<211> 370

<212> DNA

<213> Homo sapien

<400> 416

ccgacacggt	gccagcgccc	tgctgcgtgc	ccgccagcta	caatcccatg	gtgctcattc	60
aaaagaccga	taccgggggtg	tcgctccaga	cctatgatga	cttgtagcc	aaagactgcc	120
actgcataatg	agcagtcctg	gtccttccac	tggtgcacctg	cgcggaggac	gcgacctcag	180
ttgtctgcc	ctgtggaatg	ggctcaaggt	tcttgagaca	cccgattcct	gccccaaacag	240
ctgtatttat	ataagtctgt	tatttattat	taattttattg	gggtgacctt	cttggggact	300
cgggggctgg	tctgatggaa	ctgtgtattt	atttaaaact	ctggtgataa	aaataaagct	360
gtctgaactg						370

<210> 417

<211> 463

<212> DNA

<213> Homo sapien

<400> 417

acactttata	tattccaaat	tgatcagata	tatggtttgc	aaattcatct	caatctgtag	60
cttatctttt	cctcttctta	aatcacaagt	ttttaaat	tgaagaagtc	caatatatca	120
gattttgtct	tttatggatg	tgctttcggg	gcaaagtcca	agaacttgtc	acctagccca	180
agatcctgaa	gatttttctc	ctgtggcttt	tttcaaagtt	atctagtttt	atgtatcaca	240
tttaagtcgy	ttatacat	tgagttaa	tttatataag	acgtgaggtt	taagtagagg	300
ttcttttttc	tcctcgccat	gggtgtctaa	ttgctctagc	ataatttgtc	agaaaggcta	360
ttcttctctc	attgaattgc	tttttcaact	tttcaaaatc	agctgagcat	atttatatgg	420
gtttatttct	gggttctctc	atctgttcca	ttgacgtatg	tgt		463

<210> 418

<211> 334

<212> DNA

<213> Homo sapien

<400> 418

ttagcatttg	cttttatttt	tttactttga	tgctttttca	aattggcatg	tctttaaagt	60
atttttcttc	ctgattaaaa	atgtgtgtgt	atgtgtgtgt	gtgtgtgtat	atatatat	120
ttttaaatca	cattaatttt	accaagtga	accaagccat	actgtttttg	agccaattaa	180
gaaaattgcc	attttttaaag	tgtagcattt	cagggtaaaag	acccatgaaa	tggcttgatg	240
tattctagac	tactgaaaga	aaaccacttc	aaagattttg	ttgaaagttt	tagtgttgtc	300
tgaatgcaa	gaggggaaggt	gattggtagt	gagt			334

<210> 419

<211> 297

<212> DNA

<213> Homo sapien

<400> 419

acttctttga	ccaaggaata	ccacagacac	cctaccgata	gaacagtggc	tcagatctta	60
cttgctcctg	cttacgaagt	attcccaatc	actggtcata	tgaccctact	tgaacactcc	120
tgaacagtca	tgttttttaa	aatcttcctt	tatatcaagt	cagagagtat	acttctataa	180
atttcactca	tggatgttag	gaaatctagt	catcttcctt	gtgattgcc	tgtaagtat	240
ttaaccatag	ctatcatgtg	tttcccaaat	cttctctaga	ttaaatactt	tcagtta	297

<210> 420

<211> 418

<212> DNA

<213> Homo sapien

<400> 420

acgagaggaa	ccgcaggttc	agacatttgg	tgtatgtcct	atcaatagga	gctgtatttg	60
ccatcatagg	aggcttcatt	cactgatttc	ccctattctc	aggctacacc	ctagacaaaa	120
cctacgccaa	aatccatttc	gctatcatat	tcctcggcgt	aaatctaact	ttcttcccac	180
aacactttct	cggcctatcc	ggaatgcccc	gacgttactc	ggactacccc	gatacataca	240
ccacatgaaa	tatcctatca	tctgtaggct	cattcatttc	tctaacagca	gtaattattaa	300
taattttcat	gatttgagaa	gccttcgctt	cgaagcgaaa	agtcctaata	gtagaagaac	360
cctccataaa	cctggagtga	ctatatggat	gccccccacc	ctaccacaca	ttcgaaga	418

<210> 421

<211> 304

<212> DNA

<213> Homo sapien

<400> 421

acgcctggac	ccctgtgact	tgcagcctat	cttctgatgac	atgctccact	ttctaaatcc	60
tgaggagctg	cgggtgatgg	aagagattcc	ccaggctgag	gacaaactag	accggctatt	120
cgaaattatt	ggagtcaaga	gccaggaagc	cagccagacc	ctcctggact	ctgtttatag	180
ccatcttcct	gacctgctgt	agaacatagg	gatactgcat	tctggaaatt	actcaattta	240
gtggcagggg	ggttttttaa	ttttcttctg	tttctgattt	ttgttgtttg	gggtgtgtgt	300
gtgt						304

<210> 422

<211> 578

<212> DNA

<213> Homo sapien

<400> 422

actgtgcagg	cagattcaca	gggtgggtgt	aaagcatcca	caatggctct	ggcagcatca	60
ggatcacact	tgaaggggct	ctcagacaaa	gttgatttca	tgcaactgat	tccttttcca	120
ttcgttttct	tagtcactaa	tgctttccaa	tggctatgag	tgcttttaat	aatatcaatg	180
gcaaagtcct	tatctttaaa	ttctgcatta	aacgcaaact	cattttctgg	ttttccatca	240
ggaaccttat	acctttctaa	ccagtcacac	gtagcttcta	agtagccagg	tttcagccgt	300
ttgacatcat	tgatatcatt	ataattggct	gcatcaggat	catccacatt	aatggcaatg	360
actttccagt	cggtttcccc	ttcgtcaatc	atagccaata	tgcttagaac	tttcaattat	420
ttatttcacc	tcttgacatc	accttgcttc	caatttcaca	cacatcaatt	gggtcattgt	480
caccacaaca	gccagtatgt	ttatcattgt	gccctgggtc	ttcccaagtc	tgagggatgg	540
caccatagtt	ccagatatat	cctttatacg	ggaacaaa			578

<210> 423

<211> 327

PCT/US99/30909

```

acatgaantn nccaggccca cacagccaga cagcaacaga accaagacct agggctcttc      60
actcctgtta catcacacca tggcaatgat ttacattct ccaactgatt caaatcatat    120

```

ggcagctagg gatttggggg ctccatgttt tatttcaatt gcaagttcaa gatttctttt 180
tatctttgtg ggctga 196

<210> 427
<211> 163
<212> DNA
<213> Homo sapien

<400> 427
acagaagatc catggaggca agtgctgtca ggaaggacac tgcctccctc caccctccca 60
aatgtcacca ccaagttcct tcaggtgaga cctcacacaa tgtcaagtc tttctaggaa 120
atactaagat caggttgaga gattctgctt ggtctagtca atc 163

<210> 428
<211> 315
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(315)
<223> n = A,T,C or G

<400> 428
nactgagtan agatgctggg gaatgtgcaa tatgccttga agaattgcag cagggagata 60
ctatagcacg actgccttgt ctatgcatat atcataaagg ctgcatagat gaatggttg 120
aagtaaatag atcttgccct gagcaccctt cagattaagc gtcagcttcc tgttttatag 180
gttttcttgt cttgacaaga tgcttgaaaa accaagagga tatgaaaatc tgtctctgga 240
gaaacaaaga cgcaggcata ctccagccaga aatctgagtt ttgtgagact tggtaatata 300
gagatggaca atcgt 315

<210> 429
<211> 131
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(131)
<223> n = A,T,C or G

<400> 429
acagttaggn actagaacat ttgttaagcc tcccaaagta gngtgcattg aagattctag 60
agtgtccagc tcttgacta caaatgtaat aataacagaa taaatacact taccctgatg 120
atattgaggg t 131

<210> 430
<211> 503
<212> DNA
<213> Homo sapien

<400> 430
actgattttt aataaaagaa ataaggttca aagtttagca caacaacaca gcaataagaa 60
gctgacaact tggataaaaa tacaagaaag taacacagag cccaggctac ccattattta 120
ctgtgtgcat acaggaatgc tatacttcag atgtataaat tagagactga ttttaagtta 180

WO 00/37643

PCT/US99/30909

129

ttaatttaac tactttttgt ccactgtgct aaactaaatt ttataactaat gtgctactgc	240
gtaaacactt caaagcaatc ttcattaaaa tgctgcaaag aaaaacaaga atacacatca	300
tccaaaacta aggatgtcat tgcagttcac agtttgtata ataaataccc tccctttcaa	360
tcactactaa gatcactaca tccatctctac tcatcacttc aaccttgaag caacttatac	420
ttacaaatat tagcaatgca gccaaacatt tgttttttgc aaagcaacta gtaaaaatca	480
agaatttttaa ttaagacggg gca	503

<210> 431
 <211> 207
 <212> DNA
 <213> Homo sapien

<400> 431	
acaagtgtgg cctcatcaag ccttgcaccag ccaactactt tgcgtttaaa atctgcagtg	60
gggccgccaa cgtcgtgggc cctactatgt gctttgaaga ccgcatgac atgagtcctg	120
tgaaaaacaa tgtgggcaga ggcctaaaca tcgcctgggt gaatggaacc acgggagctg	180
tgctgggaca gaaggcattt gacatgt	207

<210> 432
 <211> 485
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(485)
 <223> n = A,T,C or G

<400> 432	
aaaaaaagta atggaaaaat gggtgcaggt ttaatcncaa aangaactta attttngtng	60
attttgtttt atctgctaaa acactaatat ctataaatat gaactgacag catcgttcta	120
aatttacttc tgaagagctg tcgagacttc aataaaatat aagcaagtta ctggatcata	180
tttatggact gctgaattaa ctaccgaaa agtatcagtt actttcaaag aacacaaaac	240
aaagtgaacg tggaaaaaag ccttctttgc aaaagtcctt ttattagtcc tatcctctaa	300
aattccaagc cacagagcct tgatattcct ggattctggt ttaagtaacc ttagttttta	360
atatgacact tgggatatgc acaatgggaa agggtaggat atgtgaacaa aatttaattt	420
cttttttcca aaggagnca ttttctttta atncatccta tccacttttg cccacttccc	480
catgt	485

<210> 433
 <211> 280
 <212> DNA
 <213> Homo sapien

<400> 433	
actgtcacta caatattaca ttctgcaaat gttattctgt tgtatcagat acaaaatttt	60
agtgaaggtat ctctaaggca catagtagaa aacaaaattg gtaattact caagttcctt	120
tcactgtgat ttggaaatga tttaatcttt atagaatgag aacctttttt ggactagctt	180
ttttattaaa atggctcaat ttgtgtgat aaggattgca ttaatattta atagtgttg	240
cttttctctt gggcacacca ttttgatcat taaccagagt	280

<210> 434
 <211> 234
 <212> DNA
 <213> Homo sapien

<400> 434

ctttgctgcg catcaggtgc ttttaagcttc ggaacaactg tgcaggattc tatttttagta	60
ttctggaagc atcattgagg aagtagtcca gtgaagttag ctctaaaaaa actctttact	120
ctaacaatta aaagaaatat gccaaaggat ccataaggga tgaataaatt attaaactat	180
taagaagttg ctataaatat gcagtgttaa ttcaataatt cataacggac tgggt	234

<210> 435

<211> 330

<212> DNA

<213> Homo sapien

<400> 435

acctcccgtg tcaccagttc ccacagaagc actgcaaaac tccacatgtc tgctgagcgt	60
ctgttttgtt ctccaggctt cttctgcaga gcttcggggg ctacccaggc aggtgcatac	120
atgcgaccag gacattggaa agagaacttg acatcagcca tgctaattcg ggcagtcagt	180
tcctcatcaa tcattacact acggctattg agtgcagtgc gtgggatgag gggtctctagt	240
gtgtgttaga aagccatgcc ccttgccatg tccaaagcaa acttcacagc ctgggtcttg	300
tccacgacga aattggtgcc ttcattgtat	330

<210> 436

<211> 311

<212> DNA

<213> Homo sapien

<400> 436

acaactttac aatggaattg tatttcaatg attattttga taccagatta aaccttccaa	60
aaagttacac ataattcagg tctatttttt ctaccagtaa gagttctgct aaattacaaa	120
accccataat cacagtgttc agttttttaa aaattaaaca cacagtaatc ctgtcaatgt	180
taatcaaat caaaacttcg gaatgccgtg gcatttatgt gaccaatctg agtttttagat	240
acaaatacca gctgtttatc ccattgaacca tttttcctag gctgaggctg tgaaaaatcg	300
aaagtcggcg t	311

<210> 437

<211> 355

<212> DNA

<213> Homo sapien

<400> 437

actagtggat gggggtcagg gtgtcactcc aaggccctct acagaccagc agaagaggaa	60
agtcaaaaaa gccagatatg agactgctga agtgggtgta agaaatatag gcaaggtaaa	120
gggaacaaga tctgggctcc ctctacttg tgctccctac tggacctcag acacctacc	180
tctaagactg gttcttagaa ggctgaacag taaggagcat tccaatagct tctgaaactc	240
ccaaggctgt ttcaagtagt cgaaagccat cctggactg ttcagggtgc ttttctattt	300
cccacctgag ctctctgccc tttcttttag cctcacaggt ttccagaatt acagt	355

<210> 438

<211> 431

<212> DNA

<213> Homo sapien

<400> 438

acagtaactt taactttaca tagagctgag ataaaaataa agctttctta caaattacat	60
tttttttcca gtgaattact ttgcagtaa aaatagctgc tacataaatc cctcctgac	120
tctgaaaagg agttgcatat ttccaaaaat aatattctta ttttaatcac acagaagaac	180

WO 00/37643

PCT/US99/30909

131

```

gtggagcaca ggaaggaaat ggctgggtgg tcagagagag gtgagctgtc ggagaaacac    240
agttaaaacta aaaaataaaaa tccattttgt gtataaaactg acttaaacgc atgcaaagaa    300
gtggaaaaaca tatgccattt gtcaagaaaa atactgcttt atagctttta ctttacaatt    360
aaaggagaaa gcagaggcca gatataagcc cagataataa catttaagtt tctcataaaa    420
ctcccaaatg t                                     431

```

<210> 439

<211> 170

<212> DNA

<213> Homo sapien

<400> 439

```

actgtcataa aaaacagtgg agctctgtat tagaaagccc ctcagaactg ggaaggccag    60
gtaactctag ttacacagaa actgtgacta aagtctatga aactgattac aacagactgt    120
aagaatcaaa gtcaactgac atctatgcta catattatta tatagtttgt    170

```

<210> 440

<211> 400

<212> DNA

<213> Homo sapien

<400> 440

```

acgtaaaaag aacatccttc ccatcttcaa ggtcaagatt gaacgctgac tccctgcagga    60
agtcttccag gattcccagg caggaatgat ggctcctgt ccctgtagct ccaggagttc    120
ttgcttcacg cagcctcac ataccagact gaatgttggc aggaggagt accaggtcgg    180
tcctctgtgt ccctaccacc tacaacaggc cagcaatcta cccgtgtgtg tttgttgagc    240
agaattaacc atgatgggag gccgagggcg cctggagcta tttgggggct tggagagaac    300
ctcttaggag agtgtcaggc tctaggccag tctcaccaga ggaggtcagt ctcagtcctt    360
ggagtgggtg gatggaaacc agacgggact ggcattggtcc    400

```

<210> 441

<211> 204

<212> DNA

<213> Homo sapien

<400> 441

```

acctagttac ttcttaagat caggtgtata aaactgtgga gtggagcggg atggtatgga    60
atgacttgga atgtaagctg tcagggagaa aatgttgtta cacttttgct aagatctggg    120
ggtttcttca tattcctgct gttggaagca gttgaccaga aatgcttgcc agtactgcca    180
aagcactgct gtgaaatgtg aagt                                     204

```

<210> 442

<211> 649

<212> DNA

<213> Homo sapien

<400> 442

```

acatttaatt ttttacaaca ttttctccct agagatataa tttagatatt cctatcttca    60
aagtaaaaaa caaaaatagga aataagcata gaaacagcct attggcagtg gttacacctg    120
catggtattt atgagtctcc aaactattgg aaatattttt caaccaaggt tctcttaagt    180
cttcattact tgggtgtaac tcgagagaaa actaattttat atcaatttac agtttagtgg    240
tcattgatcag ggyaaagtga tactcttcca ctgactacaa gtcattgcag aggcagttta    300
gaacttttcc tttattccta atatacagga caaaccttgc cgacatctca ctacctcaa    360
aatcaaattt aaatgaagta tccaggagta gcctaaagaa tgagtgtaat ctggatggat    420
tttagtctaa atttatgcct tgctcttcag taaagtatag taactccaga tatatgttcc    480

```

acagatgcaa taatttctgt tccttggtcg gtgcagaata taatttatac ttcttgaaat 540
caactttgtc tattcatgaa aatagctgct ttttatttgc ctttgtctca ctttgaatat 600
atatgatcca caggttacag acttttccaa taactacatt tcaacttgt 649

<210> 443
<211> 346
<212> DNA
<213> Homo sapien

<400> 443
acgtgggatt gaaatgcaca tacatgtttt tgctaagagc acatacattt cattctcctc 60
actttgttca taacctcagc attgtcagat aacctcagtg agttaactca aagcctttta 120
ttatggaaag aactggcaca gttacatttg ccagtggcaa catccttaaa aattaataac 180
tgatgggtca cggacagatt ttgacctag ttcttttttc ttttagagca aaaagaactt 240
ttacctggc atccagccca acccctaaag actgacaata tccttcaagc tcctttgaaa 300
gcacctaaa cagccatttc cattttaata gttggatgcg gattgt 346

<210> 444
<211> 425
<212> DNA
<213> Homo sapien

<400> 444
accaatttcc ttttacagta aaggggcttt tctgtgtgct tgttgaaccg gttcccagct 60
gccattacc accaagccca aaagagtaaa ttctgctctg tgaaggaaca aaagcagaag 120
tgtgtgcgcg tccacaagca atctcagtg caatgcttcc cataagttca aaaactttcc 180
ttgggtttat ttcatgactg gtagaattat ggcccaactg accataccct ccagctccaa 240
aagtaaacac tccaccttcc ttggtttagag cagcagtatg atcttctcca caacaaatat 300
aaactatfff ctgagatctt agtgacttta gtaaattagg aacataccta tcattttcat 360
cattaagacc tagctgacca aacttggttg gtcccatcc aaagatagct ccagaaaggg 420
tgagt 425

<210> 445
<211> 210
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (210)
<223> n = A,T,C or G

<400> 445
nactgtccca atataaaaca gtaattattt gacctttgca ctgtttgtct ggtccttttc 60
agtttgattg catataaatg tggaacttga tagatctcta tatttttaat gcacttgtga 120
taactggca gcagggttag acattacttt caaagcttga ggtagaccga gtcagcatgc 180
tagacaggct tctctctcta accaaaactg 210

<210> 446
<211> 326
<212> DNA
<213> Homo sapien

<400> 446
tcgaaagacc cctgtaaaag agcccaacag tgaaaatgta gatatcagca gtggaggagg 60

```

cgtgacaggc tggagagca aatgctgctg agcattctcc tgttccatca gttgccatcc 120
actaccccggt tttctcttct tgctgcaaaa taaaccactc tgcccatttt taactctaaa 180
cagatatttt tgtttctcat cttaactatc caagccacct attttaattg ttctttcatc 240
tgtgactgct tgctgacttt atcataattt tcttcaaaca aaaaaatgta tagaaaaatc 300
atgtctgtga gttcattttt aaatgt 326

```

<210> 447

<211> 304

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(304)

<223> n = A,T,C or G

<400> 447

```

nntcnaggt acatgctaga agtctgatgt ngtnngtaac acagaaacat acacagtctt 60
catattcaaa gtcttcacng ggatgtcgtt ctgtaatttc ctgcgttttg gtctcttcca 120
gaaacagctt tagcttcctg ctccgaaggc caaacacctt ggctgcttca tacagaagac 180
cttggtgggt gagtccattc tgcccaagtg ggttttcaag caggagagtg cccactgtcc 240
ccattaaaca ctcttggtgc ttgcatcca ggagctgtag gttgatatac tgacaaggaa 300
gagt 304

```

<210> 448

<211> 203

<212> DNA

<213> Homo sapien

<400> 448

```

acatgaaagc ggcaatgcgg taaaaagcga attcttacct aaggtcagaa ttttttatta 60
agcgcatttt cattagttgg acaacaacc ttataaacc ttatgtcaaa ccatataatg 120
tgaagaatct ccatgggaga gattttttt cacccttcag aattatcttt ttcccctaag 180
accttcatat gaatcttctt tgt 203

```

<210> 449

<211> 481

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(481)

<223> n = A,T,C or G

<400> 449

```

acttgttcta taatactctg atgtttcctt aaattcctga acaacattct gtttactaaa 60
tttcttttct tcctttattc acaccaaat ccaccctata atagaagcta attatttcag 120
aaagcttttt agtgatcatt tattactttg tgtttactag atattaattc taagatgaat 180
tcctttagaa ttttagaaaa aattattcta gacaacaatc aaagtaaagg atacatccag 240
cattgaaacc ataagccggc aagtctccag gttaaaagg ttgtatctc cagcaatgcc 300
agactgtgtc agacatctct gcaattcatc agcatctatc tgccatcct gtccagctac 360
agcagcaaag taaccatata gcggatcctg agtttgcct ggaaacgcag gccctccggg 420
agccccctca tactgcatct tgagttgaag tcttatangt agaagctggg gatccttaga 480
g 481

```

<210> 450
<211> 296
<212> DNA
<213> Homo sapien

<400> 450
acatggttta atacaacaac aaaaaaattt aatcaagtga aacgtaataa actgaacaat 60
aaacactcaa aacattttcc attggaaaca tgtaaagaca atatgagggt ttgttaccat 120
cttactgcaa ttttcttatg tgttactagt ctacataccc catgttttct gtaatcatgc 180
agatgtgaat ggaagtttga atgattaaat aaatgaaaag tccgtttact gcagggaatc 240
atttcacaag gcagccaaac cgggtttaga gaacaaaact attcaagaaa ttctcc 296

<210> 451
<211> 294
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(294)
<223> n = A,T,C or G

<400> 451
acatgntcca aggcacgcgn ctgtgaactt cctctgagtg aaggcatccc ctccagcacc 60
tttcagcctg ctagttagga cgaccgcgcg ccaccctcca ggacctccag cctgcactg 120
cctttcctct cttttaaata attcttcatt gagttcta atgtaaaaaa aaagtttact 180
gtaaagtgtg caaataanga aatttttttt aaaagtcctc agtaatctta ccagtaacaa 240
ttgttatggg cacatttgct tttggaagat ttcttttgta tgcattggat aagt 294

<210> 452
<211> 129
<212> DNA
<213> Homo sapien

<400> 452
acttttagat cacaaatttg cttttaagta acacataata cacttaaggc agatttgcct 60
tacagggtgc ctcagcttct aaacaccact acactgcttt atataaaaaa caaaaatcac 120
atagaagag 129

<210> 453
<211> 151
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(151)
<223> n = A,T,C or G

<400> 453
actctcaann tgtatttagg tgccaacaca tttaggatca ttgnngnttc tcagtgaatt 60
gaccttttta tgagaataaa atgtctattt ctgaaatgtc cctattttctg gaaatgttcc 120
ttatactaaa gtccaacttg tgtggattan t 151

<210> 454
<211> 119
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(119)
<223> n = A,T,C or G

<400> 454
tgctgatgna gcatgctttt taaatccctt aaaaacactc accatataaa cttgcatttg 60
agcttggtgtg ttcttttgtt aatgtgtaga gttctccttt ctcgaaattg ccagtgtgt 119

<210> 455
<211> 515
<212> DNA
<213> Homo sapien

<400> 455
accttataaa gttccttttc atccttctct gtcttcaact gacattcaag ttgttctctt 60
tcattgtgtg ccttcttgag ttggccttt aaactgtcta attcggtttc tttttcaatt 120
gctttatgtg ttactgacac aatatcttcc tcaagctgat gggctttgga tgtagcatca 180
ctgaacctct tcttaaaactc ttcattttcc atttttaagc ttgtgtttac ttcagtaaga 240
cccttttgtt ctgcttgacg ttggtcacat ctttctttct catggttaag ttctctttcc 300
attctcccaa cttgttctcg aagttgtgct gtttcttttt ccagaacggc aattaacttt 360
aacagttctt ctttttcttt catggttttc tcaattttca actcaagaag gcctgctttt 420
gtggtcacca ctaacatgtc agaatttcc tcatcttcca tagtaagcag ctcttcaact 480
ggagaagaag ctcgaaactg gaaaggtgta cctgc 515

<210> 456
<211> 350
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(350)
<223> n = A,T,C or G

<400> 456
actccctccc ccaaataga acctcaaaga ctgattcatt tcccctaggg cctgggccag 60
gagtagtca ctgctcactg ctgaggagaa aggcacaaga tataatgtca taagagcagg 120
acagtggctc agcctacaga gttccctata ggggaaagaa ggcaggaaat aggcgcaggg 180
tctggtcctg tccctgcacc accctgagca gctagtcttg ggaagggatt acaggccctg 240
ggccataggc tgctcgccat tctgctttcc tctcctgttt ctctccctgt gctgctccct 300
tttagccagn gctgagaaat gttcancacc tgaggcaaaa ctgccatagt 350

<210> 457
<211> 293
<212> DNA
<213> Homo sapien

<400> 457
gcagggccaa cagtcacagc agccctgacc agagcattcc tggagctcaa gctcctctac 60

WO 00/37643

PCT/US99/30909

136

aaagaggtgg	acagagaaga	cagcagagac	catgggaccc	ccctcagccc	ctccctgcag	120
attgcatgtc	ccctggaagg	aggctcctgct	cacagcctca	cttctaacct	tctggaaccc	180
acccaccact	gccaaagctca	ctattgaatc	cacgccattc	aatgtcgcag	aggggaagga	240
ggttcttcta	ctcgcaccaca	acctgcacca	gaatcgtatt	ggttacagct	ggc	293

<210> 458
 <211> 500
 <212> DNA
 <213> Homo sapien

<400> 458						
actagactcc	agattaccct	ttcttaataa	atatctcagg	gtaaggaaag	aaagaaactg	60
tatagatata	ttttaaataag	agaatacttt	ccaagcaata	catgatgcct	ttcctaataag	120
actctaaaag	aaaaagattc	tgtaactctc	ttttagcacc	aaattattgt	ttatcttgct	180
ggatatttta	tatgaacagt	gttaattttag	atgcactaaa	gcaaaggtag	gcaaactaca	240
accatgagtc	aaacatggcc	acacccattc	atttgctatt	gtctaagctg	gttttgact	300
acaactgcag	agttgaatag	atgcagcaga	tcctttacag	aaaaagtttt	ctgacctcaa	360
ttctaaagta	attgtagtag	ggagctggag	gactttcttt	ccctttatgg	taattttttg	420
agctacaaaa	agagccttgc	agaaatgggt	gaagggatta	atctttttaa	aataaatgct	480
atatattagg	aaaaataaaa					500

<210> 459
 <211> 394
 <212> DNA
 <213> Homo sapien

<400> 459						
ggtgaaaaga	cttgatTTTT	tgaaaggatt	gtttatcaaa	cacaattcta	atctcttctc	60
ttatgtatTT	ttgtgacta	ggcgcagttg	tgtagcagtt	gagtaatgct	ggtagctgt	120
taaggtggcg	tggtgcagtg	cagagtgcct	ggctgtttcc	tggtttctcc	cgattgctcc	180
tgtgtaaaga	tgcttgctcg	tgcaaaaaca	aatggctgtc	cagtttatta	aaatgcctga	240
caactgcact	tccagtcacc	cgggccttgc	atataaataa	cggagcatac	agtgagcaca	300
tctagctgat	gataaataca	cctttttttc	cctcttcccc	ctaaaaatgg	taaatctgat	360
catatctaca	tgtatgaact	taacatggaa	aatg			394

<210> 460
 <211> 279
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(279)
 <223> n = A,T,C or G

<400> 460						
actnccgatt	gaagccccc	ttcgtataat	aattacatca	caagacgtct	tgcaactcatg	60
agctgtcccc	acattaggct	taaaaacaga	tgcaattccc	ggacgtctaa	accaaaccac	120
tttcaccgct	acacgaccgg	gggtatacta	cggcfaatgc	tctgaaatct	gtggagcaaa	180
ccacagtttc	atgcccatcg	tcctagaatt	aattccccca	aaaatctttg	aaatagggcc	240
cgtattttacc	ctatagcacc	ccctctagag	caaaaaaaa			279

<210> 461
 <211> 278
 <212> DNA

<213> Homo sapien

<400> 461

tttggacact	aggaaaaaac	cttgtagaga	gagtaaaaaa	tttaacaccc	atagtaggcc	60
taaaagcagc	acccaattaa	gaaagcggtc	aagctcaaca	cccactacct	aaaaaatccc	120
aaacatataa	ctgaactcct	cacacccaat	tggaccaatc	tatcaccta	tagaagaact	180
aatgttagta	taaagtaaca	tgaaaacatt	ctcctccgca	taagcctgcg	tcagattaaa	240
acactggact	gacaattaac	agccaatatc	tacaatca			278

<210> 462

<211> 556

<212> DNA

<213> Homo sapiens

<400> 462

aacgtccaag	ggggccacat	cgatgatggg	caggcgggag	gtcttggtgg	ttttgtattc	60
aatcactgtc	ttgccccagg	ctccggtgtg	actcgtgcag	ccatcgacag	tgacgctgta	120
ggtgaagugg	ctgttgccct	cggcgcggtg	ctcgatctcg	ttggagccct	ggaggagcag	180
ggccttcttg	aggttgccag	tctgctggtc	catgtaggcc	acgctgttct	tgcagtggta	240
ggtgatgttc	tgggagccct	cggtaggacat	caggcgcagg	aaggtcagct	ggatggccac	300
atcggcaggg	tcggagccct	ggccgccata	ctcgaactgg	aatccatcgg	tcatgctctc	360
gccgaacccg	acatgcctct	tgtccttggg	gttcttgcgt	atgtaccagt	tcttctgggc	420
cacactgggc	tgagtggggt	acacgcaggt	ctcaccagtc	tccatgttgc	agaagacttt	480
gatggcatcc	aggttgccagc	cttggttggg	gtcaatccag	tactctccac	tcttccagtc	540
agagtggcac	atcttg					556

<210> 463

<211> 659

<212> DNA

<213> Homo sapiens

<400> 463

cacactgtgc	ccttccagtt	gctggcccgg	tacaaaggcc	tgaacctcac	cgaggatacc	60
tacaagcccc	ggatttacac	ctcgcacc	tggagtgcct	ttgtgacaga	cagttcctgg	120
agtgacgga	agtcacaact	ggtctatcag	tccagacggg	ggcctttggg	caaataattc	180
tctgattact	tccaagcccc	ctctgactac	agatactacc	cctaccagtc	cttccagact	240
ccacaacacc	ccagcttctc	cttccaggac	aagagggtgt	cctgggtccct	ggtctacctc	300
cccaccatcc	agagctgctg	gaactacggc	ttctcctgct	cctcggacga	gtccctgtc	360
ctgggcctca	ccaagtctgg	cggctcagat	cgcaccattg	cctacgaaaa	caaagccctg	420
atgctctgcy	aagggtctct	cgtggcagac	gtcaccgatt	tcgagggtg	gaaggctgcg	480
attcccagtg	ccctggacac	caacagctcg	aagagcacct	cctccttccc	ctgcccggca	540
gggcacttca	acggttcccy	cacggtcac	cgcctctct	acctgaccaa	ctcctcaggt	600
gtggactaga	cggcgtggcc	caagggtggt	gagaaccgga	gaacccaggy	acgccctca	659

<210> 464

<211> 695

<212> DNA

<213> Homo sapiens

<400> 464

accttcattt	gaccccatca	gcttcagggc	cttctttaca	tttccactgg	cctgatccat	60
gtatgcaatg	ctatttttgc	agtgatatgt	gatgttctgg	gaagctcggc	tggagagaag	120
tcgaaggaat	gccagctgca	catcaaggac	atcttcagga	agttcaggat	tgccgtagct	180
aaactgaaaa	ccaccatcca	tggactctcc	aaaccaaacy	tgtttcttct	cagcactaga	240
atctgtccac	cagtgtttcc	gtggaacatt	caaaggattg	gcacttatgc	atgtttcccc	300

agtttccata ttacagaata ccttgatagc atccaatttg catccttggc taggggtcaac 360
ccagtattct ccaactctga gttcaggatg gcagaatttc aggtctctgc agtttctagc 420
gggggttttta cgagaaccat caggactaat gaggctttct atttgtccat taacagactt 480
gagtgaagtc ataatctcat cgggtgttgat tttgaaatcc attggttcat ctccataata 540
cgggggcaaaa ccgccagctt tttcacctcc aatcccagca atggcagcgg ctccaacacc 600
accacagcaa ggaccagggg caccaggagg tccaggaggg cctggttgcc ctgggtggcc 660
tggggagccc tcagatcttc tttcacctct gttac 695

<210> 465

<211> 73

<212> DNA

<213> Homo sapiens

<400> 465

cagggtccaga gctcccaggt ttcagggttg cagtcctctc agtcccagag ctcccagggt 60
ttcggtttcc agt 73

<210> 466

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 466

agcactggca gaggnagcca aatatagtga tgtgcgccag agataagtat tctcctctcc 60
aagcatattg ctatacaaga ctttaaagac ttcataaaaag ccaaacttgc agagtccctg 120
catggagtag ccaaggaaaag tcggagccca tccttttagc aaaccacgaa caccatcttc 180
tttaagtgtg actgagaatc cgttaaatat gcccttgtag ttttgggggt ccacctgcat 240
acggcatttc actaaatcca ggggaaccac agcagtgtgt gtcagaccac aacttaagac 300
cccaccaaag ccacacagtg cataatactt cgcggagcca aattcacaac tgtactcttc 360
cacggcgccg gctgccaggt tgcgagggcg gcgaggctgg cccgtgggcc ctggggagct 420
gctgcggagg tccccgagac catcgtgcac canctgcaga tgtggcggtg tgaaggggtt 480
cgcccgcgcc aggtgcgcc cggacga 507

<210> 467

<211> 183

<212> DNA

<213> Homo sapiens

<400> 467

cctcatgagc taccggggcca gctctgtact gaggtccacc gtctttgtag gggcctacac 60
cttctgagga gcaggaggga gccaccctcc ctgcagctac cctagctgag gagcctgttg 120
tgaggggcag aatgagaaaag gcaataaagg gagaaagaaa aaaaaaaaaa aaaagggcgg 180
ccg 183

<210> 468

<211> 129

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
<222> (1)...(129)
<223> n = A,T,C or G

<400> 468
gcggccgcgt cgaccggcgc cgtcggggcnc cgggcccgggc catggagctg tggacgtgtc 60
tgggccgcggc gctgctgttg ntgntgctgn tgggtgcagtt gagccgcncn gccgagttct 120
acnccaang 129

<210> 469
<211> 243
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(243)
<223> n = A,T,C or G

<400> 469
gcggccgcgt cgacnngcca tggagactgt ggcacagtag actgtagtgt gaggctcgcg 60
ggggcagtggt ccatggaggc cgtgctgaac gagctgggtgt ctgtggagga cctgctgaag 120
tttgaaaaga aatttcagtc tgagaaggca gcaggctcgg tgtccaagag cagcagttt 180
gagtagcctt ggtgcctggt gcggagcaag tacaatgatg acatccgtaa aggcacgtgt 240
ctg 243

<210> 470
<211> 452
<212> DNA
<213> Homo sapiens

<400> 470
cctcaagtac gtccggcctg gtgggtgggtt cgagcccaac ttcattgctct tcgagaagtg 60
cgagggtgaac ggtgcggggg cgcaccctct ctccgctctc ctgcgggagg ccctgccagc 120
tcccagcgac gacgccaccg cgcttatgac cgaccccaag ctcatcacct ggtctccggt 180
gtgtcgcaac gatgttgctt ggaactttga gaagtccctg gtgggcccctg acggtgtgcc 240
cctacgcagg tacagccgcc gcttccagac cattgacatc gagcctgaca tcgaagccct 300
gctgtctcaa gggctcagct gtgcctaggg cgccctcctt accccggctg cttggcagtt 360
gcagtgtctg tgtctcgggg gggttttcat ctatgagggg gtttcctcta aacctacgag 420
ggaggaacac ctgattctac agaaaatacc ac 452

<210> 471
<211> 168
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(168)
<223> n = A,T,C or G

<400> 471
cttctccgct cttctetanga tctccgctg gtccggncgc cctgcctcca ctccctgcctc 60
taccatgtcc atcagggtga cccagaagtc ctacaagggtg tccacctctg gccccggggc 120
cttcagcagc cgctcctaca cgagtggggc cggttcccgcc atcagctc 168

<210> 472
<211> 479
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1) ... (479)
<223> n = A,T,C or G

<400> 472
gccaggcgtc cctctgtctg ccaactcagt ggcaacaccc gggagctggt ttgtcctttg 60
tggagcctca ncagttccct ctttcanaac tcactgccca gagccctgaa caggagccac 120
catgcagtgc ttcagcttca ttaagaccat gatgatcctc ttcaatttgc tcactcttct 180
gngtggcgca gccctgttgg cagcgggcat ctgggtgnca atcgatgggg cactccttct 240
gaagatcttc gggccactgt cgtccactgc catgcagttt qtcaacgngg gctacttcct 300
catcgcagcc ggcgttgtgg tntttgctct tggtttctct ggctgctatg gtgctaana 360
tgagagcaag tgtgccctcg tgacgntctt cttcatcctc ctctctctct tcattgctga 420
ggntgcagnt gctgaggtcc gccttggtgt acaccacaat ggctgagccc ttncctgacn 479

<210> 473
<211> 69
<212> DNA
<213> Homo sapiens

<400> 473
gagcgatgga gcgtgggtag ggagggtcca cagtgtccac tggccgtgtg cgaagggtga 60
ctcggtagt 69

<210> 474
<211> 155
<212> DNA
<213> Homo sapiens

<400> 474
gccgccactg ccgggagagc tggatgggct tctcctgcgc gccgcccggg gtctggccga 60
gtccagagag ccgcggcgcc tggttccgag gagccatcgc cgaagcccga ggcggggtcc 120
cgggttgggg actgcagggg aaggcagcgg tggcg 155

<210> 475
<211> 282
<212> DNA
<213> Homo sapiens

<400> 475
ggcttcgacg ttggccctgt ctgcttctctg taaactccct ccatcccaac ctggctccct 60
ccraccacaac caactttccc cccaacccgg aaacagacaa gcaacccaaa ctgaaccccc 120
tcaaaagcca aaaaatggga gacaatttca catggacttt ggaaaatatt tttttccttt 180
gcattcatct ctcaaaactta gtttttatct ttgaccaacc gaacatgacc aaaaacccaa 240
agtgcattca accttaccaa aaaaaaaaaa aaagggcggc cg 282

<210> 476
<211> 434
<212> DNA

<213> Homo sapiens

<400> 476

```
ctccaggaca gcgtccagct tgggtgctgt gaagacgaag tggagcggat ggttgtagaa 60
acgagtgatg gtgctgagcg gcgtgcagtc ttctgggatcc acgaaggcca agtccttgag 120
gtagagcatg tccacgatgt tggagcgctc ctctcgtac accgggatgc gcgtgtggcc 180
gctctgcatg atgctggcca ggacgccgaa gtccagcacg gtgctggcgt ccagcatgaa 240
gcagtcttcg aggggctga gcacgtctc cacggtcgg cagcgcagca cgccttgct 300
gagatcgctg taggggtcgc cgccgccg cgccagctcc agcaccgct cccgcagccg 360
cccgggccgc gccgccagct ccagcagctg cccacgggc agcgcgacgg gcagagttag 420
caggacggcc aggc 434
```

<210> 477

<211> 314

<212> DNA

<213> Homo sapiens

<400> 477

```
ggcgggcgct agctggctcc gggcagctcg gccttggggg ctctggggcc ccgagacgcg 60
gggcgtatga gtggggcggt cgctccacgc ggaagtcgga gcctcctccc ctggataggg 120
tgtacgagat ccctggactg gagcccatca cctttgcggg gaagatgcac ttctgtccct 180
ggctggcgcg gccgatcttt ccgcctcggg accgcggcta caaggacca aggttctacc 240
gctcgcctcc tcttcacgag catccgctgt acaaagacca ggctgctat atctttacc 300
accgttgccg cctt 314
```

<210> 478

<211> 317

<212> DNA

<213> Homo sapiens

<400> 478

```
aacagagtga tcattccagt taagcggggc gaagagaata cagactatgt gaacgcattcc 60
tttattgatg gctaccggca gaaggactcc tataacgcca gccagggccc tcttctccac 120
acaattgagg acttctggcg aatgatctgg gagtggaaat cctgctctat cgtgatgcta 180
acagaactgg aggagagagg ccaggagaag tgtgccagct actggccatc tgatggactg 240
gtgtcctatg gagatattac agtggaaactg aagaaggagg aggaatgtga gagctacacc 300
gtccgagacc tctgggt 317
```

<210> 479

<211> 171

<212> DNA

<213> Homo sapiens

<400> 479

```
aggtgctttg ctagatgctg tgacaggtat gccaccaaca ctgctcacag cctttctgag 60
gacaccagtg aaagaagcca cagctcttct tggcgtatct atactcactg agtcttaact 120
tttcaccagg ggtgctcacc tctgccccta ttgggagagg tcataaaatg t 171
```

<210> 480

<211> 65

<212> DNA

<213> Homo sapiens

<400> 480

```
ccccagtggt aaggctccca ccctggtaga tgaacagccc ctggagaact acctggatat 60
```

ggagt

65

<210> 481

<211> 207

<212> DNA

<213> Homo sapiens

<400> 481

```
cacagcgtgc tctgcgggggt cactcccact ttgttagtga tgtgggttatc tcctcagatg 60
gccagtttgc cctctcaggc tcctgggatg gaacctgcg cctctgggat ctcacaacgg 120
gcaccaccac gaggcgattt gtgggccata ccaaggatgt gctgagtgtg gccttctcct 180
ctgacaaccg gcagattgtc tctggat 207
```

<210> 482

<211> 319

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(319)

<223> n = A,T,C or G

<400> 482

```
cacactgtgc ccttcagtt gctggcccgg taaaaggcc tgaacctcac cgaggatacc 60
tacaagcccc ggatttacac ctgcgccacc tggagtgcct ttgtgacaga cagttcctgg 120
agtgcacgga agtcacaact ggtctatcag tcagacggg ggcctttggt caaatattct 180
tctgattact tccaagcccc ctctgactac agatactacc cctaccagtg cttccaaact 240
gcacaacacc cnagcttctt cttccagnac aagaggggtgt cctggteccct ggcctacctc 300
cccaccatcc agagctgct 319
```

<210> 483

<211> 233

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(279)

<223> n = A,T,C or G

<400> 483

```
acaggcccag tggcgccctag ccttcagctg ctgggctctc ccgagcctgc cttagcccat 60
acaaccaact gatcacgcgg gcattgcgct ccaccaccga cacgccatag ggaacgcgct 120
cccggggccc ctctcaaca gtcaccgagc tgcggcgagg gcagccccct tcagagctgc 180
ccggcccagc actgggccct gccagggaca cnatatccga gctggcccgt gcc 233
```

<210> 484

<211> 194

<212> DNA

<213> Homo sapiens

<400> 484

```
agagcccttg ctgggggggtg cctgggagat ggggtaagaa gagctttcat ttgtctggta 60
gatagatagc atgtaagggg gtggttgctc caggaggcag ctgctgacag gtttgctaca 120
```


cacagccccg gactgtgttg cctgggtgct cattcagaga ggggctatca tctgggagcc 180
tgtgcccctg ggtc 194

<210> 485

<211> 67

<212> DNA

<213> Homo sapiens

<400> 485

tccatatcca ggtagttctc caggggctgt tcacttacca gggtagggagc ctcccactgg 60
gggaagt 67

<210> 486

<211> 70

<212> DNA

<213> Homo sapiens

<400> 486

taccgagtca accttcgcac acggcgagtg gacactgtgg accctcccta cccacgctcc 60
atcgctcagt 70